Part II

Uncompressed Solids Formulations

Uncompressed Solids Formulations

Acebutolol Hydrochloride Capsules

Acebutolol hydrochloride is a selective, hydrophilic beta β-adrenoreceptor blocking agent with mild intrinsic sympathomimetic activity. It is used to treat patients with hypertension and ventricular arrhythmias, and is marketed in capsule form for oral administration. The capsules are provided in two dosage strengths, which contain 200 or 400 mg of acebutolol as the hydrochloride salt. The inactive ingredients present are: D&C Red 22, FD&C Blue 1, FD&C Yellow 6, gelatin, povidone, starch, stearic acid, and titanium dioxide. The 200-mg dosage strength also contains D&C Red 28; the 400-mg dosage strength also contains FD&C Red 40.

Aceclofenac Instant Granules

Bill of Materials			
Scale (mg/Sachet)	**Item**	**Material Name**	**Qty/1000 Sachet (g)**
50.00	1	Aceclofenac	50.00
165.83	2	Orange Flavor	165.83
3292.30	3	Sorbital	3292.30
169.23	4	Lutrol F 68	169.23
169.23	5	Cremophor RH 40	169.23
QS	6	Deionized Water	about 2 kg

MANUFACTURING DIRECTIONS

1. Granulate Items 1–3 with a solution of Items 4–6, pass through a 0.8-mm screen, dry, and sieve again.
2. Fill 3.9 g in sachets corresponding to 50 mg aceclofenac.

Acetaminophen and Diphenhydramine Hydrochloride Hot Therapy Sachet

Bill of Materials			
Scale (mg/Sachet)	**Item**	**Material Name**	**Qty/1000 Sachet (g)**
1650.0000	1	Acetaminophen Micronized	1650.0000
250.0000	2	Diphenhydramine Hydrochloride	250.0000
0.9000	3	FD&C Yellow No. 10 Lake	0.9000
0.0005	4	FD&C Red No. 40	0.0005
18081.1000	5	Castor Sugar	18081.1000
200.0000	6	Aspartame	200.0000
250.0000	7	Cornstarch Dried	250.0000
180.0000	8	Citric Acid	180.0000
38.0000	9	Sodium Citrate	38.0000
200.0000	10	Sodium Chloride	200.0000
240.0000	11	Honey Dry Flavor	240.0000
100.0000	12	Lemon Dry Flavor	100.0000
QS	13	Purified Water	QS

MANUFACTURING DIRECTIONS

1. Items 1 and 2 are mixed well, followed by passing through sieves. Items 3, 5, and 13 are mixed and made into a clear solution.
2. Step 1 is added to Step 2 and mixed well.
3. This is added to Item 4 and mixed. Take care to avoid lump formation.
4. Dry in an oven. Sieve and add Items 6–12. Mix well.
5. Make sure all the solids added are in fine powder form. Fill 20 g powder into sachets and seal.

Acetaminophen Capsules 500 mg

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
500.00	1	Acetaminophen Powder	500.00
30.00	2	Sodium Starch Glycolate	30.00
1.00	3	Aerosil 200	1.00
2.00	4	Magnesium Stearate	2.00
17.00	5	Starch Dried	15.00

MANUFACTURING DIRECTIONS

1. Charge all items after passing through No. 60 screen mesh and mix for 1 h.
2. Fill 550 mg in size 0 capsule.

Acetaminophen, Doxylamine, and Caffeine Effervescent

Bill of Materials			
Scale (mg/Sachet)	**Item**	**Material Name**	**Qty/1000 Sachet (g)**
500.00	1	Acetaminophen Powder	500.00
5.00	2	Doxylamine Succinate	5.00
33.00	3	Caffeine (Knoll)	33.00
391.00	4	Tartaric Acid	391.00
417.00	5	Sodium Hydrogen Carbonate	417.00
6.00	6	Kollidon 30	6.00
—	7	Isopropanol (or Ethanol)	QS
30.00	8	Sodium Citrate	30.00
707.00	9	Sugar	707.00

MANUFACTURING DIRECTIONS

1. Granulate a mixture of Items 1–5 with a solution of Items 6 and 7. Dry at 60°C under vacuum conditions, sieve, and mix with Items 8 and 9.
2. Fill 2.1 g in sachets at a maximum 30% of relative atmospheric humidity. If the solvent isopropanol is replaced by water, the granulation should be done in a fluidized bed.

Acetaminophen Instant Granules

1.

Bill of Materials			
Scale (mg/g)	**Item**	**Material Name**	**Qty/kg (g)**
166.66	1	Acetaminophen Fine Powder	166.66
426.64	2	Sucrose Fine Powder	426.64
300.00	3	Kollidon CL-M	300.00
23.33	4	Aspartame	23.33
16.66	5	Orange Flavor	16.66
16.66	6	Strawberry Flavor	16.66
40.00	7	Kollidon 30	40.00
250.00	8	Ethanol 96%	250.00

MANUFACTURING DIRECTIONS

1. Granulate Items 1–6 with solution made from Items 7 and 8 and pass through a 0.8-mm sieve.
2. Fill 1.5 g or 3.0 g in sachets (for 250 or 500 mg strength, respectively). The free-flowing granules are very well dispersible in cold water. Suspend 1.5 g or 3.0 g of the granules (= 250 mg or 500 mg acetaminophen, respectively) in a glass of water.

2.

Bill of Materials			
Scale (mg/g)	**Item**	**Material Name**	**Qty/kg (g)**
192.30	1	Acetaminophen Fine Powder	192.30
500.00	2	Sorbitol Instant (Merck)	500.00
192.30	3	Kollidon CL-M	192.30
27.00	4	Aspartame	27.00
19.23	5	Orange Flavor	19.23
19.23	6	Strawberry Flavor	19.23
11.53	7	Sodium Citrate	11.53
11.53	8	Citric Acid	11.53
30.76	9	Kollidon 90 F	30.76
192.30	10	Ethanol 96%	192.30

MANUFACTURING DIRECTIONS

1. Granulate Items 1–8 with a solution made from Items 9 and 10 and pass through a 0.8-mm sieve.
2. Fill 1.3 g or 2.6 g in sachets (for 250 or 500 mg strength, respectively).
3. The free-flowing granules are very well dispersible in cold water. Suspend 1.2 g or 2.6 g of the granules (= 250 mg or 500 mg acetaminophen, respectively) in a glass of water.

3.

Bill of Materials			
Scale (mg/Sachet)	**Item**	**Material Name**	**Qty/1000 Sachet (g)**
500.00	1	Acetaminophen Fine Powder	500.00
1300.00	2	Sorbitol Instant (Merck)	1300.00
500.00	3	Lutrol F 127	500.00
30.00	4	Citric Acid Powder	30.00
30.00	5	Sodium Citrate	30.00
80.00	6	Kollidon 90 F	80.00
500.00	7	Ethanol 96%	500.00

MANUFACTURING DIRECTIONS

1. Granulate a mixture of Items 1–5 in a solution of Item 6 in Item 7. Fill 2.44 g in sachets (= 500 mg acetaminophen).
2. The free-flowing granules are very well dispersible in cold water.
3. The taste of the suspension is only slightly bitter (2.44 g in a glass of water).

Acetaminophen, Pseudoephedrine Hydrochloride, Chlorpheniramine Hot Therapy Sachet

Bill of Materials			
Scale (mg/Sachet)	**Item**	**Material Name**	**Qty/1000 Sachets (g)**
650.00	1	Acetaminophen Micronized	650.00
60.00	2	Pseudoephedrine Hydrochloride	60.00
4.00	3	Chlorpheniramine Maleate	4.00
1.20	4	Dispersed Orange	1.20
18,081.10	5	Castor Sugar	18,081.10
200.00	6	Aspartame	200.00
250.00	7	Cornstarch Dried	250.00
180.00	8	Citric Acid	180.00
38.00	9	Sodium Citrate	38.00
200.00	10	Sodium Chloride	200.00
400.00	11	Blood Orange Dry Flavor	400.00
QS	12	Purified Water	QS

MANUFACTURING DIRECTIONS

1. Items 1 and 2 are mixed well, followed by passing through sieves and adding to Items 3 and 12 premixed and made into a clear solution.
2. Take care to avoid lump formation.
3. Dry in an oven.
4. Sieve and add Items 6–11. Mix well.
5. Make sure all the solids added are in fine powder form. Fill 20 g powder into sachets and seal.

Acetaminophen, Pseudoephedrine Hydrochloride Hot Therapy Sachet

Bill of Materials			
Scale (mg/Sachet)	**Item**	**Material Name**	**Qty/1000 Sachet (g)**
650.00	1	Acetaminophen Micronized	650.00
260.00	2	Pseudoephedrine Hydrochloride	260.00
0.90	3	FD&C Yellow No. 10 Lake	0.90
18,081.10	4	Castor Sugar	18,081.10
200.00	5	Aspartame	200.00
250.00	6	Cornstarch Dried	250.00
180.00	7	Citric Acid	180.00
38.00	8	Sodium Citrate	38.00
200.00	9	Sodium Chloride	200.00
240.00	10	Apple Dry Flavor	240.00
100.00	11	Cinnamon Dry Flavor	100.00
QS	12	Purified Water	QS

MANUFACTURING DIRECTIONS

1. Items 1 and 2 are mixed well, followed by passing through sieves and added to Items 3 and 12 premixed and made into a clear solution.
2. Take care to avoid lump formation.
3. Dry in an oven.
4. Sieve and add Items 6–11. Mix well.
5. Make sure all the solids added are in fine powder form. Fill 20 g powder into sachets and seal.

Acetaminophen Swallow Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
325.00	1	Acetaminophen Fine Powder	325.00
409.50	2	Sodium Carbonate Fine Powder	409.50
13.91	3	Cornstarch	13.91
32.50	4	Starch Pregelatinized	32.50
1.30	5	Polyvinylpyrrolidone K25	1.30
0.39	6	Potassium Sorbate	0.39
9.75	7	Talc	9.75
3.25	8	Stearic Acid	3.25
23.86	9	Ac-Di-Sol®	23.86
QS	10	Water Purified	QS

MANUFACTURING DIRECTIONS

1. Sift Items 1–6 through 16-mesh sieve into a suitable mixer and granulate with a suitable quantity of Item 10 to form a medium/heavy granule.
2. Dry the granules in a suitable oven at 45°C until the water content is <1%.
3. Pass the dried granule through a 12-mesh sieve to produce a white granule (yield 20.250 kg).
4. Fill 819.46 mg in a suitable capsule size.

Acetazolamide Sustained-Release Capsules

Acetazolamide is *N*-(5-sulfamoyl-1,3,4-thiadiazol-2-yl) acetamide. The sustained-release capsules, for oral administration, each contains 500 mg of acetazolamide and the following inactive ingredients: ethyl vanillin, FD&C Blue No. 1, FD&C Yellow No. 6, gelatin, glycerin, microcrystalline cellulose, methylparaben, propylene glycol, propylparaben, silicon dioxide, and sodium lauryl sulfate.

Acetylcysteine Sachets

1.

Bill of Materials			
Scale (mg/Sachet)	**Item**	**Material Name**	**Qty/1000 Sachet (g)**
66.66	1	Acetylcysteine[a]	66.66
914.16	2	Sugar, 18 to 60 Mesh	914.16
3.33	3	Saccharin Sodium	3.33
0.66	4	Silicon Dioxide Colloidal	0.66
0.16	5	Dye FD&C Yellow No. 6	0.16
—	6	Mandarin Flavor (e.g., Naarden)	Approx. 13 ml

[a] 200 mg/sachet.

MANUFACTURING DIRECTIONS

1. Load the acetylcysteine, half the amount of sugar, and saccharin sodium into a suitable blender and premix for 30 min.
2. Sift the premix from Step 1 through an 850 µm aperture screen.
3. Load again into the blender. Add the remaining amount of sugar and colloidal silicon dioxide and blend until uniform (typically, this is achieved on the PK Processor® by heating the envelope to 40°C and mixing until the product cools to 30–35°C).
4. Dissolve the dye in 13 ml of distilled water. Continue mixing the blended powders from Step 3. When addition of the solution is complete, continue massing until the granulation is evenly wetted and colored. If necessary, complete massing with additional quantities of distilled water (approximately 1 ml increments).
5. Verify that massing is adequate. Do not overmass.
6. Spread the wet granules on trays and dry at 50°C until LOD is NMT 1% (3 h at 60°C at 5 mmHg).
7. Allow the granules to cool, then sift on an oscillating granulator fitted with a 1.18-mm aperture screen.
8. Load the granules from step above into a suitable blender, add the flavor, and blend until uniform (15 min) passing it through a 1.18-mm screen if necessary.
9. Fill into suitable sachets at a theoretical fill weight of 3.0 g per sachet.

2.

Bill of Materials			
Scale (mg/Sachet)	**Item**	**Material Name**	**Qty/1000 Sachet (g)**
66.66	1	Acetylcysteine BP (200 mg/sachet)	66.66
914.16	2	Sugar 18 to 60 Mesh	914.16
3.33	3	Saccharin Sodium	3.33
0.66	4	Silicon Dioxide Colloidal	0.66
0.16	5	Dye FD&C Yellow No. 6	0.16
—	6	Mandarin Flavor (e.g., Naarden)	Approx. 13 ml

MANUFACTURING DIRECTIONS

1. Load the acetylcysteine, half the amount of sugar, and saccharin sodium into a suitable blender and premix for 30 min.
2. Sift the premix from Step 1 through an 850-µm aperture screen. Load again into the blender.
3. Add the remaining amount of sugar and colloidal silicon dioxide and blend until uniform (typically, this is achieved on the PK Processor® by heating the envelope to 40°C and mixing until the product cools to 30–35°C).
4. Dissolve the dye in 13 ml of distilled water. Continue mixing the blended powders from Step 3. When addition is complete, continue massing until the granulation is evenly wetted and colored. If necessary, complete massing by additional quantities of distilled water (approximately 1 ml increments). Verify that the massing is adequate, and note the total quantity of added water. Record total quantity of water added.
5. Do not overmass. Spread the wet granules on trays and dry at 50°C until LOD is NMT 1% (3 h at 60°C at 5 mmHg).
6. Allow the granules to cool, then sift on an oscillating granulator fitted with a 1.18-mm aperture screen.
7. Load the granules from Step 6 into a suitable blender, add the flavor, and blend until uniform (15 min), passing it through a 1.18-mm screen mesh if necessary.
8. Fill into suitable approved sachets at a theoretical fill weight of 3.0 g per sachet.

Acitretin Capsules

Acitretin, a retinoid, is available in 10-mg and 25-mg gelatin capsules for oral administration. Chemically, acitretin is all-*trans*-9-(4-methoxy-2,3,6-trimethylphenyl)-3,7-dimethyl-2,4,6,8-nonatetraenoic acid. It is a metabolite of etretinate and is related to both retinoic acid and retinol (vitamin A). Each capsule contains acitretin, microcrystalline cellulose, sodium ascorbate, gelatin, black monogramming ink, and maltodextrin (a mixture of polysaccharides). Gelatin capsule shells contain gelatin, iron oxide (yellow, black, and red), and titanium dioxide. They may also contain benzyl alcohol, carboxymethylcellulose sodium, and edetate calcium disodium.

Acrivastine and Pseudoephedrine Hydrochloride Capsules

Acrivastine and pseudoephedrine hydrochloride is a fixed combination product formulated for oral administration. Acrivastine is an antihistamine and pseudoephedrine is a decongestant. Each capsule contains 8 mg of acrivastine and 60 mg of pseudoephedrine hydrochloride, and the following inactive ingredients: lactose, magnesium stearate, and sodium starch glycolate. The green and white capsule shell consists of gelatin, D&C Yellow No. 10, FD&C Green No. 3, and titanium dioxide. The yellow band around the capsule consists of gelatin and D&C Yellow No. 10. The capsules may contain one or more parabens and are printed with edible black and white inks.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
8.00	1	Acrivastine	8.00
60.00	2	Pseudoephedrine	60.00
440.00	3	Lactose	440.00
5.00	4	Magnesium Stearate	5.00

MANUFACTURING DIRECTIONS

1. Blend Items 1–3 after sifting through an 80-mesh screen.
2. Pass Item 4 through a 100-mesh screen and add to Step 1; blend for 2 min.
3. Fill 513 mg in size 0 capsules.

Acyclovir Capsules

Acyclovir is a synthetic nucleoside analog that is active against herpes viruses. The chemical name of acyclovir is 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]-6 *H*-purin-6-one. Each capsule contains 200 mg of acyclovir and the inactive ingredients cornstarch, lactose, magnesium stearate, and sodium lauryl sulfate. The capsule shell consists of gelatin, FD&C Blue No. 2, and titanium dioxide. It may contain one or more parabens and is printed with edible black ink.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
200.00	1	Acyclovir, USE Acyclovir Micronized	212.00
3.00	2	Sodium Lauryl Sulfate	3.00
20.00	3	Cornstarch	20.00
52.00	4	Lactose Monohydrate	52.00
2.00	5	Magnesium Stearate	2.00
—	6	Ethanol	60 ml

MANUFACTURING DIRECTIONS

1. Charge Items 1–4 in a suitable mixer and mix for 5 min with slow chopper speed.
2. Add Item 6 slowly with mixing at slow speed; mix and chop for 2–3 min.
3. Check for satisfactory massing; use additional Item 6 if necessary.
4. Spread granules to 1/4-inch thick layer on paper trays and dry at 50°C for 4 h to a moisture of not more than 1%; dry further if required after testing.
5. Pass the dried granules through a granulator equipped with a 0-mm sieve.
6. Pass Item 5 through 250-µm sieve and add to Step 5, mix for 3 min.
7. Use size 1 capsules to fill 289 mg.

Adenosine Monophosphate Topical Powder

Bill of Materials			
Scale (mg/g)	**Item**	**Material Name**	**Qty/kg (g)**
30.00	1	DBcAMP[a]	30.00
920.00	2	Polyethylene Glycol 6000	920.00
30.00	3	Talc	30.00
20.00	4	Colloidal Silica Aerosil 200	20.00

[a] Sodium N^6, 2′-O-dibutyryladenosine-3′,5′-cyclic phosphate.

MANUFACTURING DIRECTIONS

1. Pass all items through a 100-mesh sieve and blend.
2. Pack in a bottle. Topical powder for treatment of dermatosis.

Aluminum Acetate Powder

Each powder packet, when dissolved in water and ready for use, provides the active ingredient aluminum acetate, resulting from the reaction of calcium acetate (938 mg), and aluminum sulfate (1191 mg). The resulting astringent solution is buffered to an acid pH.

Aluminum Hydroxide and Magnesium Carbonate Dry Syrup

Bill of Materials			
Scale (mg/g)	**Item**	**Material Name**	**Qty/kg (g)**
200.00	1	Aluminum Hydroxide Dry Gel (Giulini)	200.00
200.00	2	Basic Magnesium Carbonate	200.00
240.00	3	Kollidon CL-M	240.00
211.50	4	Sorbitol, Crystalline	211.50
41.30	5	Orange Flavor	41.30
82.60	6	Kollidon 30	82.60
3.30	7	Coconut Flavor	3.30
4.13	8	Banana Flavor	4.13
4.13	9	Saccharin Sodium	4.13
8.26	10	Water	8.26

MANUFACTURING DIRECTIONS

1. Granulate mixture of Items 1–5 with solution of Items 6–10, pass through a sieve, and dry. Shake 58 g of the granules with 100 ml of water.

Aminosalicylic Acid Granules

Delayed release granule preparation of aminosalicylic acid (p-aminosalicylic acid:4-aminosalicylic acid) for use with other anti-tuberculosis drugs for the treatment of all forms of active tuberculosis due to susceptible strains of tubercle bacilli. The granules are designed for gradual release to avoid high peak levels that are not useful (and perhaps toxic) with bacteriostatic drugs. Aminosalicylic acid is rapidly degraded in acid media; the protective acid-resistant outer coating is rapidly dissolved in neutral media so a mildly acidic food, such as orange, apple, or tomato juice, or yogurt or applesauce, should be consumed. Aminosalicylic acid (p-aminosalicylic acid) is 4-amino-2-hydroxybenzoic acid. PASER granules are the free base of aminosalicylic acid and do NOT contain sodium or sugar. With heat p-aminosalicylic acid is decarboxylated to produce CO_2 and m-aminophenol. If the airtight packets are swollen, storage has been improper. Supply warning: DO NOT USE if packets are swollen or the granules have lost their tan color and are dark brown or purple. The granules are supplied as off-white, tan-colored granules with an average diameter of 1.5 mm and an average content of 60% aminosalicylic acid by weight. The acid-resistant outer coating will be completely removed after a few minutes at a neutral pH. The inert ingredients are: colloidal silicon dioxide, dibutyl sebacate, hydroxypropyl methylcellulose, methacrylic acid copolymer, microcrystalline cellulose, and talc.

Amlodipine Besylate and Benazepril Hydrochloride Capsules

The capsules are formulated for oral administration with a combination of amlodipine besylate equivalent to 2.5 mg or 5 mg of amlodipine and 10 mg or 20 mg of benazepril hydrochloride. The inactive ingredients of the capsules are calcium phosphate, cellulose compounds, colloidal silicon dioxide, crospovidone, gelatin, hydrogenated castor oil, iron oxides, lactose, magnesium stearate, polysorbate 80, silicon dioxide, sodium lauryl sulfate, sodium starch glycolate, starch, talc, and titanium dioxide.

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
20.00	1	Benazepril Hydrochloride	20.00
32.92	2	Lactose Monohydrate	32.92
5.00	3	Pregelatinized Starch	5.00
1.00	4	Colloidal Silica	1.00
2.00	5	Crospovidone	2.00
10.00	6	Microcrystalline Cellulose	10.00
4.00	7	Hydrogenated Castor Oil	4.00
—	8	Water Purified	QS
4.88	9	Hydroxypropyl Methylcellulose 2910, 3 cps	4.88
0.12	10	Polysorbate 80	0.12
—	11	Water Purified	QS
QS	12	Talc	QS
5.00	13	Amlodipine, USE Amlodipine Besylate	6.94
124.05	14	Microcrystalline Cellulose, Avicel PH102	124.05
63.00	15	Dibasic Calcium Phosphate	63.00
4.00	16	Sodium Starch Glycolate	4.00
2.00	17	Magnesium Stearate	2.00

MANUFACTURING DIRECTIONS

1. Mill Items 1–3 and blend together.
2. Add water (Item 8) to granulate the blend.
3. Screen the wet granules and dry them in oven.
4. Mill the dried granules and then mill together with Items 5–7.
5. Screen Item 4 and mix in Step 4.
6. Compress into a core.
7. Dissolve Item 10 in Item 11 and add Item 9 to it.
8. Coat the core prepared in Step 6 using Item 12 to dust the cores.
9. Mix Items 13–16, then blend and screen; blend again in a separate vessel.
10. Screen Item 17 separately and add to Step 9.
11. Fill in size 1 hard gelatin capsules the coated cores with 200 mg of the powder in Step 10.

Amlodipine Besylate Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
5.00	1	Amlodipine, USE Amolodipine Besylate	7.00
93.00	2	Microcrystalline Cellulose, Avicel PH102	93.00
65.00	3	Dibasic Calcium Phosphate	65.00
8.00	4	Sodium Starch Glycolate	8.00
0.50	5	Colloidal Silicon Dioxide Aerosil 200	0.50
1.50	6	Magnesium Stearate	1.50
1	7	Empty Hard Gelatin Shell, Size 3	1000

MANUFACTURING DIRECTIONS

1. Sift amlodipine besylate, Avicel PH102, Dibasic calcium phosphate and Primojel® through a 0.500-mm sieve, and mix well in a mixer.
2. Lubricate the powder mixture in Step 1 with magnesium stearate and aerosil 200 that has been previously sieved. Mix for 2 min to get a homogeneous powder.
3. Fill the capsule in the capsule-filling machine to a weight adjusted to provide 5 mg amlodipine per capsule.

Amoxicillin and Bromhexine Hydrochloride Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
250.00	1	Amoxicillin, USE Amoxicillin Trihydrate	290.00
8.00	2	Bromhexine, USE Bromhexine Hydrochloride	8.80
34.00	3	Starch Dried	34.00
3.00	4	Magnesium Stearate	3.00
3.50	5	Aerosil 200	3.50
40.00	6	Talc	40.00
1	7	Hard Gelatin Capsule, Size 1	1000.00

MANUFACTURING DIRECTIONS

1. Charge Items 1 and 3–6 in a suitable blender and mix for 10 min.
2. In a separate mixer, add small portion of Step 1 and add by geometric dilution Item 2 and mix well.
3. Sift through No. 60 mesh screen.
4. Fill 398 mg in each capsule.

Amoxicillin and Clavulanic Acid Powder for Suspension, 125 mg and 31.25 mg per 5 ml

Amoxicillin is a semisynthetic antibiotic and an analog of ampicillin, with a broad spectrum of bactericidal activity against many gram-positive and gram-negative microorganisms. Chemically, it is (2 *S,*5 *R,*6 *R*)-6-[(*R*)-(-)-2-amino-2-(*p*-hydroxyphenyl)acetamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid trihydrate. Each capsule, with a royal blue opaque cap and pink opaque body, contains 250 mg or 500 mg of amoxicillin as the trihydrate. The cap and body of the 250-mg capsule are imprinted with the product name and 250; the cap and body of the 500-mg capsule are imprinted with AMOXIL and 500. The inactive ingredients are: D&C Red No. 28, FD&C Blue No. 1, FD&C Red No. 40, gelatin, magnesium stearate, and titanium dioxide.

Bill of Materials

Scale (mg/g)	Item	Material Name	Qty/kg (g)
19.00	1	Amoxicillin Trihydrate	19.00
10.60	2	Potassium Clavulanate (eq. Clavulanic Acid) 1:1 in Sylloid	10.60
15.00	3	Aerosil 200	15.00
48.80	4	Mannitol	48.80
0.50	5	Citric Acid Monohydrate	0.50
1.90	6	Sodium Citrate	1.90
1.20	7	Xanthan Gum	1.20
2.00	8	Powdered Flavor	2.00
0.45	9	Sweetener	0.45

MANUFACTURING DIRECTIONS

1. Charge Items 1–9 after passing through a No. 60 screen mesh at a temperature of 25°C and relative humidity of not more than 30% in a suitable blender-mixer.
2. Fill 5 g in a 30-ml bottle. Reconstitution with water gives 125 mg of Item 1 and 31.25 mg of Item 2 per 5 ml.

Amoxicillin and Clavulanate Potassium for Suspension

This is an oral antibacterial combination consisting of the semisynthetic antibiotic amoxicillin and the (beta)-lactamase inhibitor, clavulanate potassium (the potassium salt of clavulanic acid). Amoxicillin is an analog of ampicillin, derived from the basic penicillin nucleus, 6-aminopenicillanic acid. Chemically, amoxicillin is (2S,5R,6R)-6-[(R)-(-)-2-amino-2-(*p*-hydroxyphenyl)acetamido]-3, 3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid trihydrate. Clavulanic acid is produced by the fermentation of *Streptomyces clavuligerus*. It is a β-lactam structurally related to the penicillins and possesses the ability to inactivate a wide variety of (beta)-lactamases by blocking the active sites of these enzymes. Clavulanic acid is particularly active against the clinically important plasmid-mediated (beta)-lactamases that are frequently responsible for transferred drug resistance to penicillins and cephalosporins. Chemically clavulanate potassium is potassium (Z)-(2R,5R)-3-(2-hydroxyethylidene)-7-oxo-4-oxa-1-azabicyclo [3.2.0]-heptane-2-carboxylate. The inactive ingredients are: powder for oral suspension (i.e., colloidal silicon dioxide, flavorings, succinic acid, xanthan gum, and aspartame) hydroxypropyl methylcellulose, mannitol, silica gel, silicon dioxide, and sodium saccharin.

Bill of Materials

Scale (mg/Bottle) (7 g/60 ml)	Item	Material Name	Qty/1000 Bottle (g)
1500.00	1	Amoxicillin Trihydrate (equivalent to 1,250 g of Amoxicillin)	1500.00
393.60	2	Potassium Clavulanate	393.60
150.00	3	Xanthan Gum	150.00
1800.00	4	Hydroxypropyl Methylcellulose Dried	1800.00
150.00	5	Saccharin Sodium	150.00
300.00	6	Silicon Dioxide Colloidal	300.00
10.00	7	Succinic Acid	10.00
1500.00	8	Silica Gel	1500.00
183.60	9	Peach Dry Flavor	183.60
236.40	10	Strawberry Dry Flavor	236.40
731.14	11	Lemon Dry Flavor	731.14

Note: 156 mg/5 ml syrup 60 ml (125 mg amoxicillin and 31.25 mg clavulanic acid.) 6.95 g/60 ml: Each 5 ml of reconstituted syrup contains 156.25 mg of amoxicillin and clavulanic acid.

MANUFACTURING DIRECTIONS

Note: Throughout the process of manufacturing and filling maintain RH of NMT 40%.

I. Preparation of Powder Mix
   A. Mill 50% of Amoxicillin Trihydrate, Saccharin Sodium (dried to NMT 2% moisture by Karl Fischer method), Succinic Acid through a 250-µm sieve or using a Fitz mill or equivalent with blades forward. Transfer to a blending mixer and mix for 15 min.
   B. Mill remaining Amoxicillin Trihydrate through a #100 mesh using a Fitz mill or equivalent and mix with above screened powders, mix for 15 min.
   C. Mill Xanthan Gum, Hydroxypropyl methylcellulose (dried to NMT 2% moisture dried at 105EC for 2 h), Colloidal Silica, and Silica Gel through a No. 250-µm sieve or using Fitz mill or equivalent with knives forward. Add to above mixture in Step B and mix for 15 min at medium speed.
   D. Screen all dry flavors through a 250-µm mesh screen and add to above mixture from Step C.

II. Finishing
   A. Fill dry powder about 7 g in dry 60-ml glass bottles at a fill weight based on the assay of the active constituent.

Amoxicillin Powder for Suspension 125 and 250 mg

Bill of Materials			
Scale (mg/5 ml)[a]	**Item**	**Material Name**	**Qty/5 l (g)**
125.00	1	Amoxicillin, USE Amoxicillin Trihydrate with 8% Excess	143.50
1.04	2	Simethicone A	1.04
111.11	3	Castor Sugar	111.11
444.44	4	Castor Sugar	444.44
2479.86	5	Castor Sugar	2479.86
23.33	6	Sodium Citrate	23.33
1.67	7	Xanthan Gum	1.67
13.33	8	Blood Orange Dry Flavor	13.33
0.74	9	Vanilla Dry Flavor	0.74
4.44	10	Orange Banana Dry Flavor	4.44
14.44	11	Aerosil 200	14.44

[a] After reconstitution.

MANUFACTURING DIRECTIONS

1. Charge Item 3 and Item 2 in a mixer and mix for 2 min.
2. Add Item 4 and Items 6–11 and mix for 5 min.
3. Pass through Fitz mill; impact forward at high speed using sieve 24228.
4. In a separate mixer, charge Item 5 and Item 1 and mix well, passing through a sifter.
5. Add to Step 3 and mix for 20 min.
6. Fill 65 g for 100-ml and 39 g for 60-ml pack size.

Amoxicillin Trihydrate Capsules 250 and 500 mg

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
500.00	1	Amoxicillin, USE Amoxicillin Trihydrate	576.00
1.20	2	Aerosil 200	1.20
7.72	3	Magnesium Stearate	7.72
8.91	4	Sodium Lauryl Sulfate	8.91

MANUFACTURING DIRECTIONS

1. All operations are to be completed at relative humidity 40–45% and temperature 20–25°C.
2. Pass Item 1 through 1.0-mm sieve in a mixing vessel.
3. Pass Items 2–4 after passing through 250-μm sieve; add one-third portion of Item 1 from Step 2 and mix for 10 min; add another one-third Item 1 and mix and, finally, add balance and mix.
4. Fill 594 mg in size 0 capsules.

Ampicillin Powder for Suspension

Bill of Materials			
Scale (mg/5 ml)	**Item**	**Material Name**	**Qty/5 l (g)**
125.00	1	Ampicillin, USE Ampicillin Trihydrate 8% excess	144.25
1.00	2	Simethicone A	1.00
138.90	3	Castor Sugar	138.90
27.44	4	Sodium Citrate	27.44
7.00	5	Xanthan Gum	7.00
15.00	6	Blood Orange Dry Flavor	15.00
0.78	7	Vanilla Dry Flavor	0.78
7.55	8	Strawberry Dry Flavor	7.55
10.00	9	Aerosil 200	10.00
138.90	10	Castor Sugar	138.90
2747.90	11	Castor Sugar	2747.90

MANUFACTURING DIRECTIONS

1. All operations should be completed in a relative humidity of 45–55% and a temperature of 23–25°C.
2. Charge Items 2 and 3 in a suitable blender, and mix for 5 min.
3. Charge Items 1 and 4–10 in a separate mixer, and mix for 5 min.
4. Add Step 2 into Step 3, and mix for 10 min.
5. Add Item 11, and mix for 10 min.
6. Fill 65 g for a 100-ml pack and 39 g for a 60-ml pack. For 250 mg strength, adjust active ingredient, and adjust with Item 11.

Ampicillin Trihydrate Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
500.00	1	Ampicillin, USE Ampicillin Trihydrate compacted	582.13
1.17	2	Aerosil 200	1.17
11.69	3	Magnesium Stearate	11.69

MANUFACTURING DIRECTIONS

1. Pass Item 1 through a 1-mm sieve into a double-cone blender, except about 5% of the quantity.
2. In a separate container, pass and collect Items 2 and 3 through a 250-μm sieve.
3. Add the balance of Item 1 retained in Step 1 into Step 2, and blend for 10 min; pass through a 900-μm sieve if necessary.
4. Add to Step 2, and blend for 10 min.
5. Fill 223.125 mg in size 0 capsules.

Ampicillin Trihydrate Capsules for Suspension

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
250.00	1	Ampicillin, USE Ampicillin Trihydrate	250.00
2.50	2	Magnesium Stearate	2.50
—	3	Gelatin Capsule, Size 2	1000.00

MANUFACTURING DIRECTIONS

1. Dry blend ampicillin trihydrate and magnesium stearate in Baker Perkins mixer; bag off into polyethylene-lined drums.
2. Fill on Zanasi AZ20 capsule filling machine. The average fill weight is 295 ± 9 mg; the average total weight is 360 mg. For a 500-mg capsule (size 0 capsules), the average fill weight is 593 ± 15 mg; the average total weight is 690 mg.

Ampicillin Trihydrate Powder for Suspension

Bill of Materials			
Scale (mg/Bottle) (15 ml)	**Item**	**Material Name**	**Qty/1000 Bottles (g)**
1500.00	1	Ampicillin, USE Ampicillin Trihydrate (assuming potency 871; adjust amount accordingly)	1722.22
3072.10	2	Sucrose (adjust amount based on Item 1 potency)	3072.10
372.53	3	Sodium Citrate Dihydrate	372.53
31.93	4	Saccharin Sodium	31.93
2.12	5	Acid Citric Anhydrous	2.12
45.23	6	Sodium Carboxymethyl Cellulose	45.23
22.61	7	Magnesium Aluminum Silicate Veegum F	22.61
7.98	8	Dye	7.98
26.60	9	Flavor	26.60
18.00	10	Sodium Benzoate	18.00
QS	11	Water Purified	400.00
Note: Simethicone 0.15% can be added to reduce foaming during reconstitution. Adjust fill volume for the final size of reconstitution container, such as 60 ml or different strength desired, e.g., 250 mg/5 ml upon reconstitution.			

MANUFACTURING DIRECTIONS

CAUTION: Handle with extreme care. Protect face and hands from amoxicillin because some individuals may be sensitive and reactions may occur.

I. Mixing
   A. Pass sugar through a 2.38-mm aperture screen using an oscillating granulator.
   B. Pass the following ingredients through a 595-µm aperture screen in a Fitz mill (high speed, impact forward): sodium citrate, acid citric, saccharin sodium, carboxymethylcellulose, amoxicillin, and magnesium aluminum silicate.
   C. Charge ingredients from Steps A and B into a suitable mixer and mix for 10 min until uniform.
   D. Dissolve yellow dye in approximately 60 g of purified water.
   E. Mass mixture from Step C with dye solution from Step D. If necessary, pass wet mass through a 4.76-mm aperture screen. *CAUTION: Do not over wet or over mass. Product must remain as wet granules.*
   F. Spread evenly on stainless steel trays. If necessary, pass wet mass through a 4.76-mm aperture screen.
   G. Oven dry granules at 45°C until loss on drying is not more than 0.6% (vacuum 60°C, 2 h).

II. Finishing
   A. Fill product into suitable containers. Theoretical fill weight is 5.32 g (+3% fill excess) per 15-ml container, requiring approximately 12 ml of water for reconstitution.

Antibacterial and Bacterial Culture Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
125.00–500 mg	1	Penicillin, Cephalosporin or Macrolide	125.00–500.00
10–100 Million	2	Lactobacillus Acidophilus[a]	10–100 B

[a] Substitute with: Lactobacillus Spores, 300–600 million; streptococcus thermophillus 10 million, Lactobacillus Lactis, 10–500 million, streptococcus lactis 10 million, saccharomyces cerevisiae 10 million, Lactobacilli GG 10^{10} units. This formulation includes both the anti-infective agent which can be penicillin, a cephalosporin or a macrolide in doses ranging from 125 to 500 mg per capsule. Also included in the same capsule is a granulation of the bacteria which are known to be eradicated during the therapy with these antibiotics. The bacterial are coated to protect them from the effect of co-administered antibiotic and last in the intestine for over 3 months replenishing the lost flora and reduce many side effects related to use of antibiotics.

MANUFACTURING DIRECTIONS

1. Granules of one of the active ingredients (e.g., microorganisms) are first prepared by the following process:

INGREDIENTS PARTS BY WEIGHT

Microorganism: 42.86%
Microcrystalline cellulose: 53.93%
Magnesium stearate: 1.07%
Colloidal silicone dioxide: 0.71%
Cross carmellose sodium: 1.43%

The granules formed are compressed into a tablet-by-tablet compression machine heaving a laying facility at a temperature below 25°C and relative humidity not more than 50%.

Tablets are transferred to a coating pan for coating using the following formulation:

INGREDIENTS PARTS BY WEIGHT

Hydroxypropyl methylcellulose phthalate: 4.37%
Titanium dioxide: 0.96%
Purified talc: 0.19%
Polyethylene glycol: 0.99%
Isopropyl alcohol: 34.95%
Dichloromethane: 58.54%

2. The remaining active ingredient (antibacterial agent) is mixed with excipients and filled into gelatin capsules. Before sealing of capsules the coated tablet containing active ingredients is introduced into capsules. The relative proportion of anti-infective agent and excipients for filling in capsule:

INGREDIENTS PARTS BY WEIGHT

Anti-infective agent: 91.94%
Pregelatinized starch: 6.24%
Magnesium stearate: 1.44%
Sodium lauryl sulfate: 0.38%

Antifungal Foot Powder

Bill of Materials			
Scale (mg/g)	**Item**	**Material Name**	**Qty/kg (g)**
5.00	1	Dichlorobenzyl Alcohol (Myacide SF)	5.00
5.00	2	Allantoin	5.00
200.00	3	Cornstarch	200.00
790.00	4	Talc	790.00

MANUFACTURING DIRECTIONS

Mix all ingredients using the geometric dilution technique and fill.

Aspartame Granules in Sachet

Bill of Materials			
Scale (mg/Sachet)	**Item**	**Material Name**	**Qty/1000 Sachet (g)**
30.00	1	Aspartame	30.00
2.00	2	Silicon Dioxide Colloidal	2.00
968.00	3	Cerelose Powder No. 60[a]	1052.00

[a] Std. Qty. of Cerelose Powder allows for Loss on Drying.

MANUFACTURING DIRECTIONS

1. Protect from moisture; 40% relative humidity (RH) at 25°C.
2. Oven dry cerelose powder at 50°C overnight until loss on drying is no more than 3% (3 h, vacuum at 60°C). Pass dried cerelose powder through 595-µm aperture screen in oscillating granulator.
3. Charge the following ingredients into suitable blender: aspartame, half the amount dried of cerelose powder (milled) and silicon dioxide colloidal. Add balance of dried cerelose powder (total amount of dried powder is 968 g/kg), and blend for 15 min.
4. Pass blended powders through 840-µm aperture screen using an oscillating granulator, and discharge into polyethylene-lined drums. Fill weight of 1 g/sachet.

Aspartame Powder in Sachet

Bill of Materials			
Scale (mg/g)	**Item**	**Material Name**	**Qty/kg (g)**
47.50	1	Aspartame	47.50
2.50	2	Silicon Dioxide Colloidal	2.50
950.00	3	Mannitol Granules	950.00

MANUFACTURING DIRECTIONS

1. Protect from high humidity; 40% RH at 25°C.
2. Pass mannitol granules and silicon dioxide colloidal through 840-µm aperture screen in oscillating granulator.
3. Charge the following ingredients into suitable blender: aspartame, half the amount of mannitol granules, and silicon dioxide colloidal.
4. Add balance of mannitol granules and blend for 15 min.
5. Pass blended powders through 840-µm aperture screen using an oscillating granulator and discharge into polyethylene-lined drums. Fill 0.8 g/sachet.

Aspirin and Chlorpheniramine Powder

The active ingredients are: aspirin (650 mg) and chlorpheniramine maleate (4 mg) per powder. The inactive ingredients are: fumaric acid, glycine, lactose, potassium chloride, silica, and sodium lauryl sulfate.

Aspirin and Phenylpropanolamine Powder

The active ingredients are: aspirin (650 mg), phenylpropanolamine hydrochloride (25 mg) per powder, and pseudoephedrine hydrochloride (60 mg) per powder sachet. The inactive ingredients are: fumaric acid, glycine, lactose, potassium chloride, silica, and sodium lauryl sulfate.

Aspirin Microencapsulated Sustained-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
320.00	1	Aspirin	320.00
480.00	2	Gelatin	480.00
QS	3	Water Purified	QS
QS	4	Corn Oil	QS
QS	5	Petroleum Ether	QS
QS	6	Isopropyl Alcohol	QS
QS	7	Glutaraldehyde 1%	QS

MANUFACTURING DIRECTIONS

1. Item 2 is added to 0.8 l of Item 3 and the mixture is allowed to stand at 25°C for 1 h while the gelatin hydrates and swells.
2. This preparation is then heated to 60°C while it is stirred at 300 rpm for 30 min; 0.5 l of distilled water, previously heated to 60°C, is then added, and the solution is stirred at 500 rpm for an additional 5 min.
3. Item 1, as finely powdered aspirin, is then added to the solution while stirring is continued to give a uniform suspension.
4. After 1 min, the warm suspension is poured without delay into 5 l of a rapidly stirred (500 rpm) solution of 20% corn oil in petroleum ether, which has been previously brought to 25°C, and the resulting emulsion is rapidly (i.e., over a period of no more than 5 min) cooled to 5°C while the stirring is continued.
5. 3.2 l of cold (5°C) isopropyl alcohol is then added to dehydrate the gelatin microspheres while the preparation is stirred for another 10 min.
6. The microspheres are then collected by filtration and washed three times with cold (5°C) isopropyl alcohol.
7. They are then immersed in 0.8 l of a 1% solution of glutaraldehyde in cold (5°C) isopropyl alcohol for 8 h and then washed three times with isopropyl alcohol, collected by filtration, and vacuum dried for 24 h.
8. The microspheres, which average 300–400 μm in diameter, are filled into gelatin capsules for administration as a safer, long-acting, analgesic product (800 mg of the microsphere mix, which contains 320 mg of aspirin, is filled into each size 0 capsule). The capsules, when released into the stomach following ingestion, provide for sustained release of the drug for from 1–4 h and also assure that the drug reaches the gastrointestinal mucosa while in the solution state, instead of the more deleterious solid state that is characteristic of conventional dosage forms of this drug. Physical integrity of the matrix is maintained for 1–4 h after the release of its drug content, after which time the matrix dissolves.

Aspirin, Salicylamide, and Caffeine Powder

Each powder contains aspirin (650 mg), salicylamide (195 mg), and caffeine (33.3 mg). The inactive ingredients are: dioctyl sodium sulfosuccinate, fumaric acid, lactose, and potassium chloride. For arthritis strength powder, the active ingredients in each powder are: aspirin (742 mg), salicylamide (222 mg), and caffeine (38 mg). The inactive ingredients are: dioctyl sodium sulfosuccinate, fumaric acid, lactose, and potassium chloride.

Azithromycin Capsules

Each capsule contains azithromycin dihydrate equivalent to 250 mg of azithromycin. The capsules are supplied in red opaque hard gelatin capsules (containing FD&C Red No. 40). They also contain the following inactive ingredients: anhydrous lactose, cornstarch, magnesium stearate, and sodium lauryl sulfate.

1.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
250.00	1	Azithromycin, USE Azithromycin Dihydrate[a]	263.00
196.00	2	Anhydrous Lactose	196.00
50.00	3	Starch (Cornstarch Dried)	50.00
9.00	4	Magnesium Stearate	9.00
2.00	5	Sodium Lauryl Sulfate	2.00
—	6	Empty Hard Gelatin Capsules, Size 0	1000

Note: Weight of one capsule = 520 mg + shell.

[a] Considering the potency of the active ingredient is 1000 mcg/mg (anhydrous basis) with water content 5.0%, the required quantity of azithromycin dihydrate depends on the provided potency.

MANUFACTURING DIRECTIONS

Note: Processing should be done under a controlled room temperature and humidity area. The limits are: room temperature: 20–25°C; RH: 40–45%.

1. Mix Items 1 and 2 in a polyethylene bag. Pass through a 500-µm stainless steel sieve. Collect in a stainless steel drum lined with a polyethylene bag.
2. Mix Items 3–5 in a polyethylene bag. Pass through a 250-µm stainless steel sieve. Collect in a polyethylene bag.
3. Take a polyethylene bag. Check if there is any leakage. Add the powder mix from Steps 1 and 2. Mix manually for 1 min.
4. Unload the powder in a stainless steel drum.
5. Check the temperature and relative humidity of the room before beginning encapsulation. The limits are: RH: 40–45%; temperature: 20–25°C.
6. Load the empty capsule shells, size 0, in the hopper.
7. Switch the power to "ON." Check the locking of the capsules without powder. The locking length is 21.1–21.7 mm.
8. Load the powder in the hopper by scoop. Switch the power to "ON." Adjust the fill net weight to 520 mg per capsule. Nominal weight of one capsule: 520 mg + weight of one empty shell (95 mg). Target weight: 520 mg ± 2% + weight of one empty shell (95 mg).

2.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
250.00	1	Azithromycin Base, USE Azithromycin Monohydrate	263.72
149.88	2	Lactose Anhydrous	149.88
9.40	3	Magnesium Stearate/Sodium Lauryl Sulfate (90/10)	9.40

Note: Based on bulk potency of 94.8%; adjust with Item 2.

MANUFACTURING DIRECTIONS

1. Sift Items 1 and 2 through an 80-mesh screen and blend.
2. Add Item 3, and mix for 3 min.
3. Fill 470 mg in size 0 capsules.

Azithromycin Capsules and Oral Suspension

Azithromycin has the chemical name (*2R, 3S, 4R, 5R, 8R, 10R, 11R, 12S, 13S, 14R)*-13-[(2,6-dideoxy-3-*C*-methyl -3-*O*-methyl-(alpha)-*L-ribo*-hexopyranosyl)oxy]-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-11-[[3,4,6-trideoxy-3-(dimethylamino)-(beta)-*D-xylo*-hexopyranosyl]oxy]-1-oxa-6-azacyclopentadecan-15-1. Azithromycin is derived from erythromycin; however, it differs chemically from erythromycin in that a methyl-substituted nitrogen atom is incorporated into the lactone ring. Capsules contain azithromycin dihydrate equivalent to 250 mg of azithromycin. The capsules are supplied in red opaque hard-gelatin capsules (containing FD&C Red No. 40). They also contain the following inactive ingredients: anhydrous lactose, cornstarch, magnesium stearate, and sodium lauryl sulfate. It is also supplied as a powder for oral suspension in bottles containing azithromycin dihydrate powder equivalent to 300 mg, 600 mg, 900 mg, or 1200 mg azithromycin per bottle and the following inactive ingredients: sucrose; sodium phosphate tribasic anhydrous; hydroxypropyl cellulose; xanthan gum; FD&C Red No. 40; and spray-dried artificial cherry, creme de vanilla, and banana flavors. After constitution, each 5 ml of suspension contains 100 mg or 200 mg of azithromycin.

Azithromycin for Oral Suspension

1.

Bill of Materials

Scale (mg/5 ml)	Item	Material Name	Qty/Bottles (g)
200.00	1	Azithromycin, USE Azithromycin Dihydrate[a]	1.263
3861.50	2	Castor Sugar	23.169
18.00	3	Tribasic Sodium Phosphate	0.108
15.00	4	Sodium Benzoate	0.090
2.50	5	Hydroxypropyl Cellulose (Klucel EF)	0.015
2.50	6	Xanthan Gum	0.015
15.00	7	Cherry Dry Flavor	0.090
33.33	8	Vanilla Dry Flavor	0.200
25.00	9	Banana Dry Flavor	0.150

[a] Considering the potency of the active ingredient is 1000 mcg/mg (anhydrous basis) with water content 5.0%, the required quantity of azithromycin dihydrate depends on the provided potency.

MANUFACTURING DIRECTIONS

Note: Processing should be done under controlled room temperature and humidity conditions. The limits are: Room temperature: 20–25°C; RH: 40–45%.

1. Dry Item 3 at 90°C for 2 h.
2. Sift Item 2 through a Fitz mill, impact forward, medium speed using sieve No. 24228.
3. Collect in a stainless steel drum.
4. Sift 12.0 g of Item 2 (From Step 2) and Item 1 through 630-µm s.s. sieve in sifter. Load into a Drum Blender. Mix for 3 min.
5. Mix 5.0 g of Item 2 (From Step 2), Item 3 from Step 1, and Items 4–9 in a polyethylene bag. Sift through 630-µm s.s sieve in sifter. Collect in a polyethylene bag.
6. Load the powder mix from Step 4 into Step 3 in a Drum Blender. Mix for 3 min.
7. Load 6.17 g of Item 2 (From Step 2) into Step 5 in a Drum Blender. Mix for 3 min.
8. The fill weight for a 30-ml pack is 25.10 g.

2.

Bill of Materials			
Scale (mg/Bottle)	**Item**	**Material Name**	**Qty/1000 Bottles (g)**
838.57	1	Azithromycin Dihydrate	838.57
15,487.74	2	Sucrose	15,487.74
70.01	3	Sodium Phosphate Tribasic Anhydrous	70.01
26.62	4	Hydroxypropyl Cellulose (Klucel EF)	26.62
26.62	5	Xanthan Gum (Keltrol)	26.62
0.67	6	FD&C Red No. 40	0.67
59.94	7	Cherry Flavor Spray-Dried Artificial No. 11929	59.94
133.28	8	Vanilla Flavor Artificial No. 11489	133.28
99.96	9	Banana Flavor Spray-Dried Artificial No. 15223	99.96

Note: Based on bulk potency of 95.4%; adjust with Item 2.

MANUFACTURING DIRECTIONS

1. Sift all ingredients through an 80-mesh screen, and mix well.
2. Fill 16.743 g per bottle.
3. To reconstitute, add 0.52 ml for each g of dry suspension.

Azithromycin Sachet for Oral Suspension

Bill of Materials			
Scale (mg/Sachet)	**Item**	**Material Name**	**Qty/1000 Sachet (g)**
1.000	1	Azithromycin Base, USE Azithromycin Dihydrate	1.048
9.707	2	Sucrose	9.707
0.088	3	Sodium Phosphate Tribasic Anhydrous	0.088
0.055	4	Colloidal Silicon Dioxide	0.055
0.038	5	Cherry Flavor Spray-Dried Artificial	0.038
0.064	6	Banana Flavor Spray-Dried Artificial	0.064

Note: Based on bulk potency of 95.4% of azithromycin; adjust for potency using Item 2.

MANUFACTURING DIRECTIONS

1. Sift Items 1–4 through an 80-mesh screen into a blender; blend.
2. Sift Items 5 and 6, and add to Step 1. Blend.
3. Fill 11 g in one sachet, approximately 3.25×4 inch, polyethylene-lined. To reconstitute, add contents to 60 ml water, and stir well.

Balsalazide Disodium Capsules

Each capsule contains 750 mg of balsalazide disodium, a prodrug that is enzymatically cleaved in the colon to produce mesalamine (5-aminosalicylic acid), an anti-inflammatory drug. Each daily dose of 6.75 g is equivalent to 2.4 g of mesalamine. Balsalazide disodium has the chemical name (E)-5-[[-4-[[(2-carboxyethyl)amino] carbonyl]phenyl]azo]-2-hydroxybenzoic acid, disodium salt, dihydrate. The inactive ingredients are colloidal silicon dioxide and magnesium stearate. The sodium content of each capsule is approximately 86 mg.

Benazepril Hydrochloride and Amlodipine Besylate Capsules

These capsules are a combination of amlodipine besylate and benazepril hydrochloride. Benazepril hydrochloride's chemical name is 3-[[1-(ethoxycarbonyl)-3-phenyl-(1S)-propyl]amino]-2,3,4,5-tetrahydro-2-oxo-1*H*-1-(3S)-benzazepine-1-acetic acid monohydrochloride. Benazeprilat, the active metabolite of benazepril, is a nonsulfhydryl angiotensin-converting enzyme (ACE) inhibitor. Benazepril is converted to benazeprilat by hepatic cleavage of the ester group. Amlodipine besylate is a white to pale yellow crystalline powder that is slightly soluble in water and sparingly soluble in ethanol. Its chemical name is (R,S)3-ethyl-5-methyl-2-(2-aminoethoxymethyl)-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5-pyridinedicarboxylate benzenesulfonate. The capsules are formulated for oral administration with a combination of amlodipine besylate equivalent to 2.5 or 5 mg of amlodipine and 10 or 20 mg of benazepril hydrochloride. The inactive ingredients of the capsules are: calcium phosphate, cellulose compounds, colloidal silicon dioxide, crospovidone, gelatin, hydrogenated castor oil, iron oxides, lactose, magnesium stearate, polysorbate 80, silicon dioxide, sodium lauryl sulfate, sodium starch (potato) glycolate, starch (corn), talc, and titanium dioxide.

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
20.00	1	Benazepril Hydrochloride	20.00
32.90	2	Lactose Monohydrate	32.90
5.00	3	Pregelatinized Starch	5.00
1.00	4	Colloidal Silicon Dioxide	1.00
2.00	5	Crospovidone	2.00
10.00	6	Microcrystalline Cellulose	10.00
4.00	7	Hydrogenated Castor Oil	4.00
QS	8	Water Purified	QS
4.88	9	Hydroxypropyl Methylcellulose 2910, 3 cps	4.88
0.19	10	Polysorbate 80	0.19
QS	11	Purified Water	QS
QS	12	Talc	QS
5.00	13	Amlodipine, USE Amlodipine Besylate	6.94
124.05	14	Microcrystalline Cellulose	124.05
63.00	15	Calcium Phosphate Dibasic	63.00
4.00	16	Sodium Starch Glycolate	4.00
2.00	17	Magenesium Stearate	2.00

MANUFACTURING DIRECTIONS

1. Benazepril hydrochloride cores are prepared using the following:
   a. Items 1–3 are milled and blended together and water is added to granulate the blend.
   b. The wet granules are screened and oven dried. The dried granules are then milled together with Items 5–7.
   c. Item 4 is screened and then mixed with the other ingredients. The resulting mixture is then compressed into a core.
2. The resulting cores are coated with a coating solution prepared as follows: Item 10 is dissolved in the water and Item 9 is added thereto.
   a. The previously made cores are then coated with this solution and the wet coated tablets are dried.
   b. The dried tablets are then dusted with Item 12.
3. Amlodipine besylate for incorporation into the formulation is prepared as follows:
   a. Items 13–16 are mixed together, and the blended mixture is screened and reblended.
   b. Item 17 is separately screened and then blended with the reblended mixture containing the amlodipine.
4. No. 1 hard gelatin capsules are used to encapsulate one benazepril hydrochloride containing coated core along with 200 mg of the amlodipine besylate containing powder per capsule.

Bisacodyl Colonic Delivery Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
210.00	1	Sugar Sphere	210.00
5.00	2	Hydroxypropyl Methylcellulose	5.00
3.00	3	Bisacodyl Micronized	3.00
1.00	4	Hydroxypropyl Methylcellulose	1.00
18.00	5	Eudragit L100-55	18.00
5.00	6	Eudragit S	5.00
4.00	7	Dibutyl Phthalate	4.00
8.00	8	Talc	8.00
1.00	9	Red Ferric Oxide	1.00
2.00	10	Talc	2.00

MANUFACTURING DIRECTIONS

1. Bisacodyl is micronized in a fluid energy mill using a grinding pressure of 50 psi to produce a powder with 90% of the particles below 10 μm.
2. It is dispersed in water at a level of 2.7% by weight, with 0.9% by weight of hydroxypropyl methylcellulose (HPMC) as a binding polymer sprayed onto sugar spheres (6.53–6.63 mm diameter) in a perforated pan coater maintaining an outlet airbed temperature of about 40°C.
3. Barrier Coat: HMPC is dissolved in water to produce a 4% by weight solution, which is coated on the substrates described above in a perforated pan coater maintaining an outlet air/bed temperature of about 40°C.
4. Inner Enteric Coat: Eudragit L100-55 and dibutyl phthalate are dissolved in a solution of isopropanol, acetone, and water (37:9:1) at levels of 8.0% and 1.6% (total weight percent), respectively. Talc is then suspended in the solution at a level of 3.3% by weight. The resulting mixture is coated onto the barrier-coated substrates in Step 4 in a perforated pan coater maintaining an outlet air/bed temperature of about 30°C.
5. Outermost Enteric Coat: Eudragit S and dibutyl phthalate are dissolved in a solution of isopropanol, acetone, and water (37:9:1) at levels of 8.0% and 1.6% (total weight percent), respectively. Red ferric oxide and talc are then suspended in the solution at levels of 1.2% and 2.1% by weight, respectively. The resulting mixture is coated onto the barrier-coated substrates above in a perforated pan coater maintaining an outlet air/bed temperature of about 30°C.
6. Appropriate theoretical quantity is filled in hard capsules.

Brompheniramine and Pseudoephedrine Capsules

These capsules are light green and clear, and contain white beads. The extended-release capsule contains: brompheniramine maleate (12 mg) and pseudoephedrine hydrochloride (120 mg) in a specially prepared base to provide prolonged action. Alternate strength is 6 mg and 60 mg, respectively. The capsules also contain the following inactive ingredients: calcium stearate, D&C Yellow No. 10, FD&C Blue No. 1, FD&C Yellow No. 6, gelatin, pharmaceutical glaze, starch, sucrose, and talc.

Budesonide Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
1.00	1	Budesonide Micronized	1.00
321.00	2	Sugar Spheres	321.00
6.60	3	Aquacoat ECD30	6.60
0.50	4	Acetyltributyl Citrate	0.50
0.10	5	Polysorbate 80	0.10
17.50	6	Eudragit L100-55	17.50
1.80	7	Triethylcitrate	1.80
8.80	8	Talc	8.80
0.01	9	Antifoam MMS	0.01

MANUFACTURING DIRECTIONS

1. Budesonide (32.2 g) is suspended in the Aquacoat ECD30 dispersion (0.70 kg) with the aid of the polysorbate 80 (0.42 g) together with acetyltributyl citrate (15.8 g).
2. The mixture is sprayed on to sugar spheres (10.2 kg) in a fluid bed apparatus.
3. The enteric coating, consisting of the Eudragit L100-55 dispersion (Eudragit L100-55 [0.558 kg], triethylcitrate [55.8 g], talc [0.279 kg], antifoam MMS [0.44 g], and polysorbate 80 [2.79 g]) is then sprayed on the spheres.
4. The pellets are dried in the fluid bed apparatus, sieved, and filled in hard gelatin capsules.

Budesonide Inhalation Powder

Budesonide is a corticosteroid designated chemically as (RS)-11(beta),16(alpha),17,21-tetrahydroxypregna-1,4-diene-3,20-dione cyclic 16,17-acetal with butyraldehyde. Budesonide is provided as a mixture of two epimers (22R and 22S). The inhalation-driven, multi-dose dry powder inhaler contains only micronized budesonide. Each actuation of container provides 200 mcg budesonide per metered dose, which delivers approximately 160 mcg budesonide from the mouthpiece (based on *in vitro* testing at 60 l/min for 2 sec).

Butalbital and Acetaminophen Capsules

Each capsule contains butalbital (50 mg) and acetaminophen (325 mg). In addition, each capsule may also contain the following inactive ingredients: benzyl alcohol, butylparaben, D&C;Red No. 28, D&C Red No. 33, edetate calcium disodium, FD&C Blue No. 1, FD&C Red No. 40, gelatin, methylparaben, propylparaben, silicon dioxide, sodium lauryl sulfate, sodium propionate, and titanium dioxide.

Calcitonin (Salmon) Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
500 IU	1	Salmon Calcitonin	500,000 IU
0.048	2	Dimyristoyl Phosphatidic Acid	0.048
3.44	3	Aprotinin[a]	3.44
3.78	4	Hydroxypropyl Cellulose-LF	3.78
3.78	5	Polyoxy-40 Stearate	3.78
140.97	6	Polyethylene Glycol 400	140.97
15.55	7	Propylene Glycol	15.55
8.83	8	Citrate Buffer	8.83
31.49	9	Cholesterol	31.49
17.40	10	Tween 80	17.40
63.69	11	Egg Yolk Lecithin	63.69
19.79	12	d-alpha Tocopherol	19.79
28.15	13	Glyceryl Monooleate	28.15
251.45	14	Isostearic Acid	251.45

Note: Human Growth Hormone: 2.6 IU = 1 mg.

[a] Aprotinin: 7500 KIU = 1 mg.

MANUFACTURING DIRECTIONS

GENERAL:

1. Polyoxy-40 stearate is dispersed in the solvent mixture of polyethylene glycol 400 and propylene glycol.
2. Sodium cholate is also separately dispersed in the mixture.
3. A water solution containing recombinant human growth hormone, phospholipid, and aprotinin is then added to the solvent mixture from Step 1, and the pH is adjusted to 2.5 with the help of buffer.
4. The lipid solution is made separately in another vessel.
5. To the oil solution, the polyol solution is added dropwise while mixing continuously. While mixing, it is suggested that the vessel be ice jacketed to prevent the denaturation of the protein in the formulation.
6. Clear transparent liquid, which is called the preemulsion solution, is obtained after approximately 5 min of mixing at low speed. An *in situ* emulsion can be made by mixing any ratio of the preemulsion solution with the simulated intestinal fluid.
7. The preemulsion solution is filled in a size 0 hard gelatin capsule, and the capsule is sealed with a band of gelatin solution. The banding helps to coat the capsule uniformly.
8. The capsule is then coated with a 10% hydroxypropyl methylcellulose solution as an undercoat. The amount of coat required is sufficient just enough to cover the capsule uniformly with a thin layer of the polymer coat. Usually, a 3.5–4.5% weight gain of the capsule is a good indication of the amount required as an undercoat.
9. Once the capsule is coated with an undercoat, enteric coating is applied. For enteric coating purposes, different polymers such as hydroxypropyl methylcellulose, hydroxypropyl methylcellulose pthalate, cellulose acetate pthalate, etc., are used.
10. Anionic copolymers, which are based on methacrylic acid and methyl methycrate and are commercially available as Eudragit, are also very suitable polymers for enteric coating purposes. The polymer is dissolved in organic solvents such as ethyl alcohol, methyl alcohol, acetone, or isopropyl alcohol. A combination of two solvents can also be used. The amount of enteric coating solution required is 5–6% of the weight gain of the capsules from the original weight of the capsules before applying enteric coat. A typical enteric coating solution is made as follows:

Methacrylic acid and methyl, 10% w/w
Methycrate copolymer (polymer)
Diethyl butyl pthalate (plasticizer), 2% w/w
Acetone, 22% w/w
Isopropanol, 66% w/w

PROCEDURE:

1. Mix acetone and isopropanol. Add the polymer slowly with constant mixing. Once the polymer is dissolved, add the plasticizer slowly and let it dissolve.
2. For a size 0 capsule the above mentioned enteric coating solution can be sprayed using fluidizing bed techniques. The fluid bed sprayer/dryer is operated with the following parameters:

   Flow Rate: 1.5 ml/min
   Inlet Air Temp: 25°C
   Outlet Air Temp: 25°C
   Air Flap: 35
   Atomizer: 2.0 bar

3. A size 0 capsule after the enteric coating will typically have the following composition:

   Preemulsion Solution: 0.589 g
   Undercoat Polymer: 0.027 g
   Enteric Coat Polymer: 0.032 g, 0.648 g

Calcitriol Capsules

Calcitriol is a synthetic vitamin D analog that is active in the regulation of the absorption of calcium from the gastrointestinal tract and its utilization in the body. Chemically, calcitriol is 9,10-seco(5Z,7E)-5,7,10(19)-cholestatriene-1(alpha),3(beta),25-triol. The other names frequently used for calcitriol are 1(alpha),25-dihydroxycholecalciferol; 1,25-dihydroxyvitamin D3; 1,25-DHCC; 1,25(OH) 2 D 3; and 1,25-diOHC. It is available as capsules containing 0.25 mcg or 0.5 mcg calcitriol and as an oral solution containing 1 mcg/ml of calcitriol. All dosage forms contain butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) as antioxidants. The capsules contain a fractionated triglyceride of coconut oil, and the oral solution contains a fractionated triglyceride of palm seed oil. Gelatin capsule shells contain glycerin, parabens (methyl and propyl), and sorbitol, with the following dye systems: 0.25 mcg of FD&C Yellow No. 6 and titanium dioxide; 0.5 mcg FD&C Red No. 3, FD&C Yellow No. 6, and titanium dioxide. The oral solution contains no additional adjuvants or coloring principles.

Calcium Carbonate Microencapsulated Sustained-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
600.00	1	Calcium Carbonate	600.00
900.00	2	Gelatin	900.00
QS	3	Water Purified	1.5 l
QS	4	Corn Oil	QS
QS	5	Petroleum Ether	QS
QS	6	Isopropyl Alcohol	QS
QS	7	Glutaraldehyde 1%	QS

MANUFACTURING DIRECTIONS

1. Item 2 is added to 1.5 l of Item 3, and the mixture is allowed to stand at 25°C for 1 h while the gelatin hydrates and swells.
2. To this mixture is added Item 1, and the preparation is heated to 60°C while it is stirred at 300 rpm for 30 min to effect dissolution of the gelatin and to ensure even suspension of the calcium carbonate. Additional distilled water, previously heated to 60°C, is then added to bring the total volume to 100°C while the stirring is continued.
3. This preparation is slowly poured into 12 l of a mixture consisting of 20% by volume of corn oil in petroleum ether, which has previously been heated to 60°C while the petroleum ether solution is stirred at 500 rpm. This preparation is then cooled to 5°C with continued stirring, and the stirring is continued at 500 rpm for 1 h after the lower temperature is reached.
4. While stirring of the preparation at 5°C is continued, 6 l of isopropanol are then added. The solid microspheres are then collected by filtration and washed three times with isopropyl alcohol. The capsules are then immersed in 1.5 L of a 1% solution of glutaraldehyde in isopropyl alcohol for 8 h at 5°C; the capsules are then washed again, three times, with isopropyl alcohol, filtered, and vacuum dried for 24 h.
5. The microspheres, which average between 200 and 300 μm in diameter, are filled into gelatin capsules for administration as a long-acting antacid product (1.5 g of the microsphere mix, which contains 600 mg calcium carbonate, are filled into each size 0 capsule). The microcapsules, when released into the stomach following ingestion, delay the reaction of the calcium carbonate with the acid of the stomach for a useful period of time (between 3 and 6 h), which provides for sustained antacid protection for the patient. Physical integrity of the matrix is maintained from 1 to 4 h after the release of its drug contents, after which the matrix dissolves through hydrolytic cleavage of its bonds and proteolytic digestion.

Camptothecin Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
100.00	1	CPT-11	100.00
470.00	2	Polyethylene Glycol 13000	470.00
50.00	3	Triacetin	50.00
5.00	4	Polysorbate 80	5.00
QS	5	Capsule Shell HPMC	1000.00

MANUFACTURING DIRECTIONS

1. Items 2–4 are melted, and Item 1 is added and admixed thoroughly; the mixture is allowed to cool and solidify.
2. Mill the Step 1 mixture into a suitable size, and fill in an HPMC shell capsule.

Carbamazepine Extended-Release Capsules

Carbamazepine is an anticonvulsant and a specific analgesic for trigeminal neuralgia, available for oral administration as 200 mg and 300 mg extended-release capsules of carbamazepine, USP. Carbamazepine is a white to off-white powder, practically insoluble in water and soluble in alcohol and in acetone. Its molecular weight is 236.27. Its chemical name is 5H-dibenz[b,f]azepine-5-carboxamide. The capsule is a multi-component capsule formulation consisting of three different types of beads: immediate-release beads, extended-release beads, and enteric-release beads. The three bead types are combined in a specific ratio to provide twice daily dosing of carbamazepine. The inactive ingredients are: citric acid, colloidal silicon dioxide, lactose monohydrate, microcrystalline cellulose, polyethylene glycol, povidone, sodium lauryl sulfate, talc, triethyl citrate, and other ingredients. The 200-mg capsule shells contain gelatin, FD&C Red No. 3, FD&C Yellow No. 6, yellow iron oxide, FD&C Blue No. 2, and titanium dioxide, and are imprinted with white ink. The 300-mg capsule shells contain gelatin, FD&C Blue No. 2, FD&C Yellow No. 6, red iron oxide, yellow iron oxide, and titanium dioxide, and are imprinted with white ink.

MANUFACTURING DIRECTIONS

This product is made from three types of pellets, one with instant-release profile and two with sustained-release profile; generally, an equal component of each pellet is used but other variations may be used as well.

	Percent	Kilograms
Pellet A: Immediate-Release Component		
Microcrystalline Cellulose, N.F. (MCC) (Avicel PH-101/102, Emcocel, etc.)	40.0	0.400
Hydroxypropyl Methylcellulose (HPMC) (Methocel E5/E50/K5/K50)	2.5	0.025
Croscarmellose, Type A, N.F. (Ac-Di-Sol)	2.0	0.020
Sodium Lauryl Sulfate (SLS)	0.1	0.001
Carbamazepine	55.4	0.554
Total	100.0	1.000
Pellet B: Sustained-Release Component		
Microcrystalline Cellulose	30.0	0.300
Hydroxypropyl Methylcellulose	5.0	0.050
Sodium Monoglycerate	8.0	0.080
Tartaric Acid	5.0	0.050
Sodium Lauryl Sulfate	0.2	0.002
Carbamazepine	51.8	0.518
Total	100.0	1.000
Coating		
Ethacrylic/Methacrylic Acid Esters (Eudragit RS100)	45.0	0.450
Ethacrylic/Methacrylic Acid Esters (Eudragit RL100)	45.0	0.450
Propylene Glycol	9.0	0.090
Talc	1.0	0.010
Total	100.0	1.000
Pellet C: Delayed-Release Component		
Microcrystalline Cellulose	25.0	0.250
Hydroxypropyl Methylcellulose Phthalate	10.0	0.100
Tartaric Acid	10.0	0.100
Sodium Monoglycerate	7.5	0.075
Dioctyl Sodium Sulfosuccinate	0.5	0.005
Carbamazepine	47.0	0.470
Total	100.0	1.000
Coating		
Cellulose Acetate Phthalate (CAP)	60.0	0.600
Ethylcellulose	25.0	0.250
PEG400	15.0	0.150
Total	100.0	1.000

Cefaclor Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
250.00	1	Cefaclor	250.00
15.00	2	Starch	15.00
5.00	3	Silicon Fluid 350 cs	5.00
4.00	4	Magnesium Stearate	4.00

Note: For 500-mg strength, fill proportionally higher quantity.

MANUFACTURING DIRECTIONS

1. Mix cefaclor with silicon fluid and magnesium stearate.
2. Slug and granulate if necessary for flow.
3. Mix with starch powder.
4. Fill in appropriate size 2 capsules. Finish capsules with polishing methods.

Cefdinir Capsules and Oral Suspension

Cefdinir capsules and cefdinir for oral suspension contain the active ingredient cefdinir, an extended-spectrum, semisynthetic cephalosporin, for oral administration. Chemically, cefdinir is [6R-[6(alpha),7(beta) (Z)]]-7-[[(2-amino-4-thiazolyl)(hydroxyimino)acetyl]amino]-3-ethenyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid. Capsules contain 300 mg cefdinir and the following inactive ingredients: carboxymethylcellulose calcium, polyoxyl 40 stearate, magnesium stearate, and silicon dioxide. The capsule shells contain FD&C Blue No. 1; FD&C Red No. 40; D&C Red No. 28; titanium dioxide, gelatin, and sodium lauryl sulfate. Powder for oral suspension, after reconstitution, contains 125 mg cefdinir per 5 ml and the following inactive ingredients: sucrose, citric acid, sodium citrate, sodium benzoate, xanthan gum, guar gum, artificial strawberry and cream flavors, silicon dioxide, and magnesium stearate. Powder for oral suspension, after reconstitution, contains 125 mg cefdinir per 5 ml and the following inactive ingredients: sucrose, citric acid, sodium citrate, sodium benzoate, xanthan gum, guar gum, artificial strawberry and cream flavors, silicon dioxide, and magnesium stearate.

Cefixime for Oral Suspension

Cefixime is a semisynthetic, cephalosporin antibiotic for oral administration. Chemically, it is (6 *R,*7 *R*)-7-[2-(2-amino-4-thiazolyl)glyoxylamido]-8-oxo-3-vinyl-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7 2-(*Z*)- [*O*-(carboxymethyl)oxime]trihydrate. Its molecular weight is 507.50 as the trihydrate.

Powder for oral suspension, when reconstituted, provides 100 mg/5 ml. The powder for oral suspension is strawberry flavored and contains sodium benzoate, sucrose, and xanthan gum.

Cefpodoxime Proxetil for Oral Suspension

Each 5 ml of oral suspension contains cefpodoxime proxetil equivalent to 50 mg or 100 mg of cefpodoxime activity after constitution and the following inactive ingredients: artificial flavorings, butylated hydroxy anisole (BHA), carboxymethylcellulose sodium, microcrystalline cellulose, carrageenan, citric acid, colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl cellulose, lactose, maltodextrin, natural flavorings, propylene glycol alginate, sodium citrate, sodium benzoate, starch, sucrose, and vegetable oil.

Cefprozil for Oral Suspension

Cefprozil is a semisynthetic, broad-spectrum cephalosporin antibiotic. Cefprozil is a cis and trans isomeric mixture (≥90% cis). The chemical name for the monohydrate is (6*R*,7*R*)-7-[(R)-2-amino-2-(p-hydroxyphenyl)acetamido]-8-oxo-3-propenyl-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid monohydrate. Cefprozil for oral suspension contains a cefprozil equivalent to 125 mg or 250 mg of anhydrous cefprozil per 5 ml of constituted suspension. In addition, the oral suspension contains the following inactive ingredients: aspartame, cellulose, citric acid, colloidal silicone dioxide, FD&C Red No. 3, flavors (natural and artificial), glycine, polysorbate 80, simethicone, sodium benzoate, sodium carboxymethylcellulose, sodium chloride, and sucrose.

Ceftibuten Capsules and Oral Suspension

Ceftibuten capsules and ceftibuten for oral suspension contain the active ingredient ceftibuten as ceftibuten dihydrate. Ceftibuten dihydrate is a semisynthetic cephalosporin antibiotic for oral administration. Chemically, it is (+)-(6R,7R)-7-[(Z)-2-(2-amino-4-thiazolyl)-4-carboxycro-tonamido]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, dihydrate. Its molecular weight is 446.43 as the dihydrate. Capsules contain ceftibuten dihydrate equivalent to 400 mg of ceftibuten. Inactive ingredients contained in the capsule formulation include: magnesium stearate, microcrystalline cellulose, and sodium starch glycolate. The capsule shell and band contain gelatin, sodium lauryl sulfate, titanium dioxide, and polysorbate 80. The capsule shell may also contain benzyl alcohol, sodium propionate, edetate calcium disodium, butylparaben, propylparaben, and methylparaben. Oral suspension after reconstitution contains ceftibuten dihydrate equivalent to 90 mg of ceftibuten per 5 ml. Oral suspension is cherry flavored and contains the following inactive ingredients: cherry flavoring, polysorbate 80, silicon dioxide, simethicone, sodium benzoate, sucrose (approximately 1 g/5 ml), titanium dioxide, and xanthan gum.

Ceftibutin for Oral Suspension

Bill of Materials			
Scale (mg/g)	**Item**	**Material Name**	**Qty/kg (g)**
72.00	1	Ceftibutin Trihydrate	72.00
0.40	2	Polysorbate 80	0.40
0.80	3	Simethicone	0.80
16.00	4	Xanthan Gum	16.00
10.00	5	Silicone Dioxide	10.00
18.00	6	Titanium Dioxide	18.00
8.00	7	Sodium Benzoate	8.00
3.66	8	Cherry Flavor, Natural and Artificial (Microencapsulated)	3.66
QS	9	Sucrose QS to 1 kg	QS

MANUFACTURING DIRECTIONS

Note: This formulation, upon reconstitution, gives a final concentration of 19 mg/ml. For 36 mg/ml, use 144.00 g of Item 1 and 4.0 g of Item 7. Adjust quantity of Item 1 based on moisture content. The quantity given here is for anhydrous form; adjust with Item 9.

1. Pass all items through an 80-mesh screen and blend.
2. Fill into 60-ml bottles at either 5, 7.5, or 15 g, or 120-ml bottles at 25 or 30 g aliquots.

Cefuroxime for Oral Suspension

Cefuroxime oral suspension contains cefuroxime as cefuroxime axetil, which is a semisynthetic, broad-spectrum cephalosporin antibiotic for oral administration. Chemically, cefuroxime axetil, the 1-(acetyloxy) ethyl ester of cefuroxime, is (*RS*)-1-hydroxyethyl (6 *R,*7 *R*)-7-[2-(2-furyl) glyoxylamido]-3-(hydroxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate, 7 2-(*Z*)-(*O*-methyl-oxime), 1-acetate 3-carbamate. The oral suspension, when reconstituted with water, provides the equivalent of 125 mg or 250 mg of cefuroxime (as cefuroxime axetil) per 5 ml of suspension. It contains the following inactive ingredients: povidone K30, stearic acid, sucrose, and tutti-frutti flavoring.

Celecoxib Capsules

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
200.00	1	Celecoxib	200.00
204.00	2	Lactose	204.00
12.00	3	Sodium Lauryl Sulfate	12.00
7.00	4	Polyvinyl Pyrrolidone Potassium 30	7.00
—	5	Isopropyl Alcohol	45.00 l
6.00	6	Polyvinyl Pyrrolidone Potassium 30	6.00
6.00	7	Magnesium Stearate	6.00
15.00	8	Talc	15.00
50.00	9	Croscarmellose Sodium	50.00

MANUFACTURING DIRECTIONS

1. Charge Items 1–3 in suitable vessel after passing through a No. 60 mesh and mix for 15 min.
2. In a separate container, mix and prepare a solution of Items 4 and 5.
3. Add Step 2 into Step 1 and mix; pass the granules through a 2.5-mm sieve; dry the granules at 40°C in open room or fluid-bed dryer to moisture of not more than 1%.
4. Pass the dried granules through a No. 30 sieve, and recycle through 1.5-mm sieve to size all granules through No. 30 mesh.
5. Pass Items 7–9 through No. 40 mesh, and add to Step 4; mix for 5–10 min.
6. Tap density is not more than 0.80 g/cc; fines are not more than 10%.
7. Fill 600 mg in size 0 capsules.

Cellulose Triacetate Liquefiable Topical Powder

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
120.00	1	Cellulose Triacetate	120.00
880.00	2	Dow Corning® 345	880.00

MANUFACTURING DIRECTIONS

1. A liquefiable powder was prepared by evaporative spray drying. Dow Corning 345, a slightly volatile cyclic silicone liquid, was used as the porogen.
2. Cellulose triacetate (40 g) was dissolved in 3000 g of methylene chloride by moderate stirring for 4 h. To that solution was added 270 g of the porogen dissolved in 1000 g of methylene chloride.
3. The resulting homogeneous solution was sprayed at 1000 PSI from a 0.0135-in. nozzle, downward into a tower 100 cm in diameter and 300 cm tall, through which 1250 l/min of solvent-free air was passing from top to bottom.
4. The evaporatively formed powder was collected on a fabric filter spanning the bottom of the tower, and the solvent-laden air was passed through carbon beds to collect and recover solvent.
5. The product was transferred to a steel tray and exposed as a 1-cm deep layer in a ventilated hood for 25 min to remove residual solvent.
6. An analysis showed 12% cellulose triacetate, 88% DC 345, and less than 4 ppm of residual methylene chloride.
7. The white powder readily could be dusted onto the feet and made to liquefy and vanish by gentle rubbing.

Cephalexin Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
500.00	1	Cephalexin, USE Cephalexin Monohydrate (0–2% excess)	526.31
2.50	2	Magnesium Stearate	2.50
QS	3	Cornstarch	600.00

MANUFACTURING DIRECTIONS

1. Charge magnesium stearate, cornstarch, and $^1/_{10}$ part of cephalexin into a suitable mixer. Mix well.
2. Pass blend from Step 1 and balance of cephalexin through an 840-µm aperture screen by hand or with a mechanical shaker.
3. Charge into a suitable mixer and mix well. Discharge into polyethylene-lined drums.
   Note: For slugging, first use 624 mg of magnesium stearate; balance after milling slugs through a 1.2-mm aperture screen in an oscillating granulator.
4. Machine fill using either size 00 or size 0 capsules; the theoretical weight of 10 caps is 6.0 g. Sort and final clean with sodium chloride.

Cephalexin Powder for Oral Suspension

Bill of Materials			
Scale (mg/5 ml)[a]	**Item**	**Material Name**	**Qty/5 l (g)**
125.00	1	Cephalexin, USE Cephalexin Monohydrate, 1.5% excess	131.50
0.50	2	FD&C No. 6	0.50
10.00	3	Orange Flavor	10.00
5.00	4	Vanilla Dry Flavor	5.00
5.00	5	Raspberry Dry Flavor	5.00
277.54	6	Castor Sugar	277.54
2844.80	7	Castor Sugar	2844.80

[a] Upon reconstitution as recommended. For 250-mg strength, adjust with Items 6 and 7.

MANUFACTURING DIRECTIONS

1. Charge Items 2–6 in a suitable mixer, and mix for 5 min.
2. Add Item 1 in portions, and mix well.
3. Pass through a Fitz mill, impact forward at high speed using sieve 24338.
4. Collect milled powder in Step 3 in a suitable mixer and mix for 10 min.
5. Pass Item 7 through 900-µm sieve; add 15% of quantity to Step 4, and mix for 10 min.
6. Load in a double-cone blender. Add the balance of Item 7 from Step 5, and mix for 20 min.
7. Fill appropriate quantity in bottles.

Cephradine Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
500.00	1	Cephradine, USE Cephradine Compacted (1000 mcg/mg with 5% moisture)[a]	526.00
7.00	2	Magnesium Stearate	7.00
8.40	3	Talc	8.40
18.60	4	Lactose Monohydrate[b]	18.60

[a] Adjust according to potency; taken as 105.2% of label.
[b] Adjust according to quantity of Item 1.

MANUFACTURING DIRECTIONS

1. Process limits are: relative humidity: 40–45%; temperature: 20–25°C.
2. Pass Item 1 through 630-µm sieve; crush larger particles in a Frewitt mill using a 1-mm sieve.
3. Load approximately half of Item 1 from Step 1 and 2 into a mixer.
4. Sift Items 2–4 through a 250-µm sieve in a suitable blender; blend for 5 min at slow speed.
5. Charge balance of Item 1 to Step 4, and blend for 5 min at slow speed.
6. Fill 560 mg per capsule.

Cephradine Powder for Suspension

Bill of Materials			
Scale (mg/5 ml)	**Item**	**Material Name**	**Qty/5 l (g)**
125.00	1	Cephradine, USE Cephradine Monohydrate with 10.8% excess[a]	131.50
8.00	2	Sodium Citrate	8.00
4.00	3	Citric Acid Anhydrous	4.00
10.00	4	Guar Gum	10.00
5.00	5	Methylcellulose, 15 cps	5.00
2.00	6	Yellow FD&C No. 6	2.00
20.00	7	Blood Orange Flavor	20.00
10.00	8	Orange Banana Flavor	10.00
3095.28	9	Castor Sugar	3095.28

[a] For 250 mg/5 ml, adjust active ingredient and adjust with Item 9.

MANUFACTURING DIRECTIONS

1. Pass Item 9 through a 500-μm sieve for use in later steps.
2. Charge Items 1–6 in a mixing vessel, and add about 10% of Item 9 from Step 1; mix for 5 min.
3. Pass the powder mixture in Step 2 through a Fitz mill.
4. Charge 10% of Item 9 from Step 1 in a separate mixing vessel, and add Items 7 and 8; blend for 5 min.
5. Add to Step 3, and blend for 5 min.
6. Pass Step 5 through a 500-μm sieve.
7. Add Item 9 (about 15%), and mix for 5 min; transfer to a double-cone blender.
8. Add 40% of Item 9, and mix for 10 min.
9. Add the balance of Item 9, and mix for another 15 min.
10. Fill. Fill weight for 100 ml = 66 g; fill weight for 60 ml = 39.60 g.

Cevimeline Capsules

Cevimeline is cis-2′-methylspiro (1-azabicyclo [2.2.2] octane-3, 5′-[1,3] oxathiolane) hydrochloride, hydrate (2:1). Each capsule contains 30 mg of active ingredient. The inactive ingredients are: lactose monohydrate, hydroxypropyl cellulose, and magnesium stearate.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
30.00	1	Cevimeline	30.00
60.00	2	Hydroxypropyl Cellulose	50.00
15.00	3	Sodium Carboxymethyl Cellulose Cross-Linked	15.00
189.00	4	Lactose	189.00
6.00	5	Magnesium Stearate	6.00

MANUFACTURING DIRECTIONS

1. Sift Items 1–3 through an 80-mesh screen and blend.
2. Pass Item 5 through a 100-mesh screen, and add to Step 1 and blend for 3 min.
3. Fill 300 mg in size 0 capsules.

Chlordiazepoxide Hydrochloride Capsules

Chlordiazepoxide hydrochloride (HCl) and the prototype for the benzodiazepine compounds provide a versatile therapeutic agent of proven value for the relief of anxiety. It is available as capsules containing 5 mg, 10 mg, or 25 mg chlordiazepoxide HCl. Each capsule also contains cornstarch, lactose, and talc. Gelatin capsule shells may contain methyl and propyl parabens and potassium sorbate, with the following dye systems: for 5-mg capsules — FD&C Yellow No. 6, plus D&C Yellow No. 10, and either FD&C Blue No. 1 or FD&C Green No. 3; for 10-mg capsules — FD&C Yellow No. 6, plus D&C Yellow No. 10, and either FD&C Blue No. 1 plus FD&C Red No. 3 or FD&C Green No. 3 plus FD&C Red No. 40; for 25-mg capsules — D&C Yellow No. 10 and either FD&C Green No. 3 or FD&C Blue No. 1.

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
5.00	1	Chlordiazepoxide Hydrochloride	5.10
114.00	2	Starch Dried	114.00
26.00	3	Dicalcium Phosphate	26.00
40.00	4	Talc	40.00

MANUFACTURING DIRECTIONS

1. Charge all ingredients in a suitable mixer after passing through a No. 60 mesh, and mix for 30 min.
2. Fill 185 mg in size 4 capsules.

Chloroxylenol and Chlorhexidine Topical Powder

Bill of Materials

Scale (mg/g)	Item	Material Name	Qty/Kg (g)
10.00	1	Chloroxylenol	10.00
10.00	2	Chlorhexidine Diacetate	10.00
30.00	3	Magnesium-L-Lactate	30.00
10.00	4	Allantoin	10.00
100.00	5	Zinc Stearate	10.00
840.00	6	Cornstarch	840.00

MANUFACTURING DIRECTIONS

1. Pass all Items through a 100-mesh screen and blend.
2. Fill; for use as a topical anti-infective formulation.

Chlorpromazine Sustained-Release Capsules

Chlorpromazine is 10-(3-dimethylaminopropyl)-2-chlorphenothiazine, a dimethylamine derivative of phenothiazine. Each sustained release capsule is so prepared that an initial dose is released promptly, and the remaining medication is released gradually over a prolonged period. Each capsule, with opaque orange cap and natural body, contains chlorpromazine hydrochloride as follows: 30 mg or 75 mg or 150 mg. Inactive ingredients consist of benzyl alcohol, calcium sulfate, cetylpyridinium chloride, FD&C Yellow No. 6, gelatin, glyceryl distearate, glyceryl monostearate, iron oxide, povidone, silicon dioxide, sodium lauryl sulfate, starch, sucrose, titanium dioxide, wax, and trace amounts of other inactive ingredients.

Cimetidine Microencapsulated Sustained-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
275.00	1	Cimetidine	275.00
525.00	2	Sodium Alginate	525.00
QS	3	Calcium Chloride 2%	QS
QS	4	Poly-L-Glycine 0.05%	QS

MANUFACTURING DIRECTIONS

1. Item 2 is dissolved in 17.5 l of distilled water at 25°C, and Item 1 is added to this solution with constant mixing.
2. This preparation is added dropwise to a 2% calcium chloride solution through a small orifice that delivers droplets that are 1.0 mm in diameter. The spherical beads of cimetidine-containing calcium alginate thus formed are collected by filtration and washed three times with distilled water.
3. The beads are then immersed in a 0.05% aqueous solution of poly-L-lysine (molecular weight 14,000) for 4 h, then washed again three times with distilled water, collected by filtration, and dried under vacuum for 24 h. The beads thus produced are filled into gelatin capsules (800 mg per capsule, providing a dose of 275 mg of cimetidine).
4. This dosage form for the delivery of cimetidine over an extended time period allows for through-the-night protection for patients who suffer from excess gastric acidity without the high bedtime dose that conventional dosage forms require for this duration of protection. The high bedtime dose otherwise required for such protection is associated with untoward side effects, which are reduced through use of the dosage form described in this example.

Citrate Effervescent Powder

Bill of Materials			
Scale (mg/Tab)	**Item**	**Material Name**	**Qty/kg (g)**
0.50	1	Oil Lemon Terpeneless	0.50
10.00	2	Flavor, Lemon Natural Microseal	10.00
QS	3	Alcohol Dehydrated	6.50
440.33	4	Sodium Bicarbonate	440.33
0.35	5	Saccharin Sodium	0.35
157.50	6	Sodium Citrate Anhydrous	157.50
178.82	7	Acid Citric	178.82
222.50	8	Acid Tartaric	222.50

MANUFACTURING DIRECTIONS

Note: All processing is in controlled humidity; maximum RH 40% at 25°C. Sodium citrate and citric acid are anhydrous.

1. Dissolve lemon oil in dehydrated alcohol with stirring in a suitable container. Delete this step if using lemon flavored powder.
2. Sift sodium bicarbonate, if necessary, through a 595-µm aperture screen, and charge into a suitable mixer or charge material into mixer and mix for 10 min.
3. Add solution from Step 1 in the mixer very slowly while mixing; continue mixing at least 10 min and up to a total of 30 min, depending on equipment.
4. Screen the massed granulation mixture through a 595-µm aperture screen.
5. Divide approx. into two halves. Premix saccharin sodium into sodium citrate (and lemon powder if used) and sift through a 595-µm aperture screen or mill with a 595-µm aperture screen, knives forward at medium speed.
6. Sift both citric acid and tartaric acid separately through a 595-µm aperture screen or mill separately using a comminuting mill with a 595-µm aperture, knives forward at medium speed.
7. Load materials into a suitable blender, preferably in the following order: milled tartaric acid, milled citric acid, half of the granulation mixture, milled saccharin sodium and sodium citrate, and the remaining granulation mixture.
8. Blend for 20 min and pack into double plastic bags inside fiber drums. Provide silica gel protection to assure low humidity in drums. If blended material is lumpy, screen through a 1.2-mm aperture screen before bagging.

Clindamycin Capsules 150 mg

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
150.00	1	Clindamycin, USE Clindamycin Hydrochloride	163.00
12.00	2	Lactose	12.00
3.00	3	Magnesium Stearate	3.00
24.00	4	Talc	24.00
2.00	5	Aerosil 200	2.00
65.00	6	Starch Dried	65.00

MANUFACTURING DIRECTIONS

1. Pass all Items through a No. 60 mesh, and mix well for 30 min.
2. Fill 270 mg in size 2 capsules.

Clofibrate Capsules

A clofibrate capsule contains ethyl 2-(*p*-chlorophenoxy)-2-methyl-propionate, an antilipidemic agent. Each Capsule contains 500 mg of clofibrate for oral administration. Capsules also contain the following inactive ingredients: D&C Red No. 28, D&C Red No. 30, D&C Yellow No. 10, FD&C Blue No. 1, FD&C Red No. 28, FD&C Red No. 40, FD&C Yellow No. 6, and gelatin.

Clonidine Sustained-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
0.10	1	Clonidine Hydrochloride (equivalent to 0.087 mg Clonidine base) 100 μm or finer	0.10
70.00	2	Methocel® E4M[a]	70.00
129.90	3	Lactulose[b]	129.90

[a] This formulation is intended to provide an 8-h release pattern; for an extended release pattern of 12 h, use Methocel® K100M.
[b] Cornstarch can be used in place of lactulose.

MANUFACTURING DIRECTIONS

1. This is a low-dose product that requires a careful geometric dilution of Item 1 with portions of Item 3.
2. Add the triturate in Step 1 in one-half of Item 3, and mix well.
3. Add Item 2, and mix well; add balance of Item 3.
4. Fill 200 mg in an appropriate capsule size.

Clorazepate Dipotassium Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
7.50	1	Clorazepate Dipotassium	7.50
10.00	2	Potassium Carbonate Dried	10.00
0.45	3	Silicon Dioxide Colloidal	0.45
168.00	4	Talc	168.00
QS	5	Sodium Chloride Granules (for cleaning)	QS

MANUFACTURING DIRECTIONS

Note: Avoid exposing clorazepate to light and moisture; process in low-humidity area (46 grains, 35% RH at 76°F).

I. Blending
   A. Determine loss on drying (1 h Brabender or equivalent at 105°C) of potassium carbonate dried (NMT 0.5%), silicon dioxide (NMT 2.5%), and talc (NMT 0.3%).
   B. Mill, while mixing the potassium carbonate and silicon dioxide through a 60-mesh (250-µm aperture) screen using a Fitz mill or a similar mill, impact forward high speed.
   C. Premix screened clorazepate with the milled mixture of potassium carbonate and silicon dioxide in a suitable container. Pass the mix through a 40-mesh (420-µm) screen by hand. Clean the screen with a small portion of talc (about 0.63 g). Use rubber gloves when handling clorazepate.
   D. Charge about half of the remaining talc into a V-blender or a similar blender. Add the preblend from Step C and, finally, the remaining talc. Blend for 30 min. Discharge into polyethylene-lined drums, tightly tie, and seal.

II. Filling
   A. Fill blended material into hard gelatin capsules; fill weight for 10 caps is 1.85 g (± 0.06 g). Sort capsules on sort vibrator, clean with sodium chloride, and store in polyethylene-lined drums.

III. Printing
   A. Print capsules using edible ink.

Cyclosporin A Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
100.00	1	Cyclosporin A	100.00
300.00	2	Cremophor RH (or Tween)	300.00

MANUFACTURING DIRECTIONS

Mix ingredients and fill in hard gelatin capsule of a type that will not interact with ingredients. Optionally, the composition may contain ethanol 8%, propylene glycol 8%, or polyethylene glycol 300, 30% by weight.

Dantrolene Sodium Capsules

The chemical formula of dantrolene sodium is hydrated 1-[[[5-(4-nitrophenyl)-2-furanyl]methylene]amino]-2, 4-imidazolidinedione sodium salt. It is supplied in capsules of 25 mg, 50 mg, and 100 mg. Each capsule contains the following inactive ingredients: edible black ink, FD&C Yellow No. 6, gelatin, lactose, magnesium stearate, starch, synthetic iron oxide red, synthetic iron oxide yellow, talc, and titanium dioxide.

Dextroamphetamine Sulfate Capsules

Dextroamphetamine is the dextro isomer of the compound *d,l*-amphetamine sulfate, a sympathomimetic amine of the amphetamine group. Chemically, dextroamphetamine is *d*-alpha-methylphenethylamine and is present in all forms of dexedrine as the neutral sulfate. Each spansule sustained release capsule is so prepared that an initial dose is released promptly, and the remaining medication is released gradually over a prolonged period. Each capsule containing 5–15 mg of active and inactive ingredients consists of: cetyl alcohol, D&C Yellow No. 10, dibutyl sebacate, ethylcellulose, FD&C Blue No. 1, FD&C Blue No. 1 aluminum lake, FD&C Red No. 40, FD&C Yellow No. 6, gelatin, hydroxypropyl methylcellulose, propylene glycol, povidone, silicon dioxide, sodium lauryl sulfate, sugar spheres, and trace amounts of other inactive ingredients.

Diclofenac and Misoprostol Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
100.00	1	Diclofenac Delayed-Release Beads (47% Diclofenac)	214.00
0.20	2	Misoprostol (dilute 1:100 on HPMC)	20.00
150.00	3	Microcrystalline Cellulose	150.00
4.00	4	Stearic Acid	4.00
9.00	5	Talc	9.00

MANUFACTURING DIRECTIONS

1. Item 1 beads are prepared by spray coating a suspension or solution of diclofenac sodium onto a nonpareil sugar core, together with a binder (e.g., polyvinylpyrollidone or hydroxypropyl methylcellulose). The beads are subsequently coated with a delayed release coating (e.g., methylmethacrylate, for example Eudragit). Mixtures of beads with various levels of coating are used to give the required therapeutic release pattern.
   a. In a fluidized-bed apparatus, uniform spherical inert sugar sphere cores are coated with a first layer consisting of the compounds, an inert water soluble polymer, such as hydroxypropyl methylcellulose or hydroxypropyl cellulose, and talc. The second layer consists of an inert water soluble polymer, such as hydroxypropyl methylcellulose or hydroxypropyl cellulose, talc, and a pigment, such as titanium dioxide. The third and enteric coating layer consists of an enteric coating polymer, such as co-polymerized methacrylic acid/methacrylic acid methyl esters, a plasticizer, such as triethy acetate or similar plasticizers, and talc. The layers are applied by conventional fluidized bed coating techniques using aqueous solutions or dispersions. Pseudo zero release is obtained by the use of a mixture of beads.
2. The beads in Item 1 contain 47% diclofenac, giving a dose per capsule of 75 mg.
3. The mixture of Items 1–4 is filled into suitable, hard gelatin capsules.

Diclofenac Sustained-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
100.00	1	Diclofenac, USE Diclofenac Sodium Pellets (520 mg/g)	192.50

MANUFACTURING DIRECTIONS

1. Fill at relative humidity that does not exceed 45% and a temperature of 20–25°C.
2. Calculate exact amount based on quantity of active ingredient in uncoated beads.
3. Fill 192.5 mg based on 100% potency basis.
4. Preparation of uncoated granules:
   a. 800 g of diclofenac sodium, 200 g of citric acid, and 200 g of cornstarch are mixed and pulverized.
   b. The fine powders thus prepared are processed to produce spherical granules, using 600 g of purified sucrose that was obtained by shifting through 20–28 mesh as a core, while spraying a solution of 25 g of hydroxypropyl cellulose in 475 g of ethyl alcohol.
   c. The granules are then dried for 3 h at 55°C.
   d. These dried granules are then passed through a 14 mesh, followed by passage through a 28 mesh. The granules that do not go through the 28 mesh are taken as uncoated granules A. The formulation of uncoated granules A is as follows:

Component	% by weight
Diclofenac sodium	43.7
Citric acid	11.0
Cornstarch	11.0
Purified sucrose	32.9
Hydroxypropyl cellulose	1.4
Total	100.0

   e. Alternate method of preparing uncoated granules:
      i. 1000 g of diclofenac sodium, 30 g of fumaric acid, and 170 g of cornstarch are mixed and pulverized.
      ii. The fine powders thus produced are processed to produce spherical granules, using 600 g of purified sucrose that is obtained by shifting through a 20–28 mesh as a core, while spraying a solution of 25 g of hydroxypropyl cellulose in 475 g of ethyl alcohol.
      iii. The granules are then dried for 3 h at 55°C.
      iv. These dried granules are then passed through a 14 mesh followed by passage through a 28 mesh. The granules that do not go through the 28 mesh are taken as uncoated granules. The formulation of this uncoated granules B was as follows:

Component	% by weight
Diclofenac sodium	54.8
Fumaric acid	1.6
Cornstarch	9.3
Purified sucrose	32.9
Hydroxypropyl cellulose	1.4
Total	100.0

5. Preparation of long-acting granules:
   a. 600 g of uncoated granules A are placed into a coating apparatus with a fluidized bed.
   b. The granules are spray-coated with 1263 g of a coating liquid having the following composition according to a conventional method to produce long-acting granules. The weight of the coat was about 8% of the weight of the uncoated granules.

Component	% by weight
Ethylcellulose	2.7
Polyvinyl pyrrolidone K30	0.9
Talc	0.2
Ethyl alcohol	96.2
Total	100.0

6. Preparation of long-acting granules, alternate method:
   a. 600 g of uncoated granules B are placed into a coating apparatus with fluidized bed.
   b. The granules are spray-coated with 1667 g of a coating liquid having the following composition according to a conventional method to produce long-acting granules.

The amount of the coat is about 20% based on the weight of the uncoated granules.

Component	% by weight
Methacrylic acid copolymer S	6.5
Glycerine fatty acid ester	0.5
Talc	0.2
Ethyl alcohol	92.8
Total	100.0

7. Preparation of long-acting granules having an exterior rapid-releasing layer:
   a. 50.7 g of diclofenac sodium and 149.3 g of cornstarch are mixed and pulverized.
   b. The fine powders thus produced are processed to produce spherical granules, using 500 g of the long-acting granules (Step 6) as a core, while spraying a solution of 4 g of hydroxypropyl cellulose in 76 g of ethyl alcohol.
   c. The granules are then dried for 2 h at 55°C to produce long-acting granules. These granules have an exterior rapid-releasing layer.

Didanosine Delayed-Release Capsules

Didanosine is given in an enteric-coated formulation of didanosine (ddl), a synthetic purine nucleoside analog active against the Human Immunodeficiency Virus (HIV). The delayed-release capsules, which contain enteric-coated beadlets, are available for oral administration in strengths of 125, 200, 250, and 400 mg of didanosine. The inactive ingredients in the beadlets include: carboxymethylcellulose sodium 12, diethyl phthalate, methacrylic acid copolymer, sodium hydroxide, sodium starch glycolate, and talc. The capsule shells contain colloidal silicon dioxide, gelatin, sodium lauryl sulfate, and titanium dioxide. The capsules are imprinted with edible inks.

Didanosine Delayed-Release Capsules Enteric-Coated Beadlets

Didanosine is the brand name for an enteric-coated formulation of didanosine (ddl), a synthetic purine nucleoside analog active against the Human Immunodeficiency Virus (HIV). Delayed-release capsules, containing enteric-coated beadlets, are available for oral administration in strengths of 125, 200, 250, and 400 mg of didanosine. The inactive ingredients in the beadlets include carboxymethylcellulose sodium 12, diethyl phthalate, methacrylic acid copolymer, sodium hydroxide, sodium starch glycolate, and talc. The capsule shells contain colloidal silicon dioxide, gelatin, sodium lauryl sulfate, and titanium dioxide. The capsules are imprinted with edible inks.

Didanosine for Oral Suspension

Didanosine (ddl) is a synthetic purine nucleoside analog active against the Human Immunodeficiency Virus (HIV). The powder for oral solution is supplied for oral administration in single-dose packets containing 100, 167, or 250 mg of didanosine. Packets for each product strength also contain a citrate-phosphate buffer (composed of dibasic sodium phosphate, sodium citrate, and citric acid) and sucrose. Pediatric powder for oral solution is supplied for oral administration in 4- or 8-ounce glass bottles containing 2 or 4 grams of didanosine, respectively. The chemical name for didanosine is 2′,3′-dideoxyinosine.

Diethyl Toluamide Topical Powder

Bill of Materials			
Scale (mg/g)	**Item**	**Material Name**	**Qty/kg (g)**
552.00	1	*N*,*N*-Diethyl-*m*-Toluamide (DEET)	600.00
368.00	2	2-Octyldodecanol	400.00
QS	3	Methylene Chloride	QS
80.00	4	Cellulose Triacetate	400.00

MANUFACTURING DIRECTIONS

1. A liquefiable powder was prepared by spray evaporative drying. A liquid porogen was prepared from 60 parts by weight of *N*,*N*-diethyl-*m*-toluamide (DEET) and 40 parts by weight of 2-octyldodecanol, a heavy secondary alcohol commonly used in cosmetic formulations.
2. Cellulose triacetate (40 g) was dissolved in 3000 gm of methylene chloride by moderate stirring for 4 h. To that solution was added 460 g of the previously prepared porogen diluted with 1000 g of methylene chloride.
3. The resulting homogeneous solution was sprayed at 1000 PSI from a 0.0135-in. nozzle, downward into a tower (100 cm in diameter × 300 cm tall), through which 1250 l/min of solvent-free air was passing from top to bottom.
4. The evaporatively formed powder was collected on a fabric filter spanning the bottom of the tower, and the solvent-laden air was passed through carbon beds to collect and recover solvent.
5. The product was transferred to a steel tray and exposed as a 1-cm deep layer in a ventilated hood for 25 min to remove residual solvent. Analysis showed 8% cellulose triacetate, 36.8% octyldodecanol, and 55.2% DEET, with less than 5 ppm or residual methylene chloride.
6. The resulting white powder could be readily dusted onto the skin and made to liquefy and vanish by gentle rubbing without any perceptible grit or gumminess.

Difluoromethylornithine-Alpha Capsules

Bill of Materials		
Item	**Material Name**	**Qty/2000 Caps (g)**
	Rapid-Release Granules	
1	Difluoromethylornithine-Alpha (DFMO)	100.00
2	Microcrystalline Cellulose (MCC) Avicel PH101	100.00
3	Water Purified	QS
	Slow-Release Granules	
4	Difluoromethylornithine-Alpha	500.00
5	Microcrystalline Cellulose PH101	500.00
6	Eudragit RS 30D	30-50
7	Triethyl Citrate	QS
8	Water Purified	QS

MANUFACTURING DIRECTIONS

1. Rapid-Release Granules: DFMO (100 g) and microcrystalline cellulose (MCC, Avicel PH101, 100 g) are mixed thoroughly. A sufficient amount of water to make a wet mass is added to the mixture, which is subsequently extruded and spheronized. The pellets are screened (size 14 to 20 mesh) and dried at 40°C for 24 h. Polyvinyl pyrrolidone (PVP, 2% by weight of total mass) can optionally be included in the formulation. Increasing PVP will generally lengthen the release profile of the formulation.
2. Slow-Release Granules: DFMO (500 g), MCC (500 g) and Eudragit (35–50 g) are mixed. To this mixture is added sufficient water to yield a 30% weight suspension. To the suspension is added triethylcitrate (10% weight based on dry polymer weight of Eudragit) to yield a dispersion that is wet granulated and dried to remove as much water as possible. The particles are then ground into a fine powder.
3. Fill the rapid-release granules (500 g prepared according) and slow release granules (750 g prepared) after thoroughly mixing.
4. Gastric-Release Granules: A slow gastric-release granule can be prepared as follows. DFMO (600 g), MCC (350 g), and HPC (50 g) are mixed thoroughly. To the mixture is added sufficient water to make a wet mass that is extruded and then spheronized using procedures well known in the art. The particles are then dried and ground.
5. Enteric-Release Granules: A latex dispersion is prepared as follows. To Eudragit L 30D-55 (1000 g, 15% weight in water) is added a plasticizer (15% weight of dry polymer weight in the Eudragit) while mixing for 1–24 h. Plasticizers, such as triethylcitrate, tributylcitrate, acetyltributylcitrate, or dibutylsebacate, can be used. To this mixture is added talc (50% weight of dry polymer in the Eudragit) or glycerylmonostearate (10% weight of dry polymer in the Eudragit) to form a dispersion. The rapid-release granules are coated in a fluidized bed with the latex dispersion until a 10–15% weight increase in granule weight is achieved. The fluidized bed inlet air temperature is adjusted to about 40–45°C. and the outlet air temperature is adjusted to about 30–35°C with a spray rate of about 2 g/min.
6. Slow-Release Granules: Granules previously prepared are coated with Eudragit L 30D (10–12% weight) or Aquateric (CAP, 10% weight, plasticized with TEC) until a 25–30% weight increase in granule weight is achieved.
7. Colorectal-Release Granules: A dispersion is prepared as follows. To Eudragit S100 (1000 g, 10% weight in water) is added a plasticizer (10% weight of dry polymer weight in the Eudragit) while mixing for 1–24 h. Plasticizers, such as triethylcitrate, tributylcitrate, acetyltributylcitrate, or dibutylsebacate, can be used. To this mixture is added talc (50% weight of dry polymer in the Eudragit) to form a dispersion. The rapid release granules previously prepared are coated in a fluidized bed with this dispersion until a 15% weight increase in granule weight is achieved.
8. Slow-Release Granules: A mixture is prepared as follows. Eudragit RS 30D (1000 g, 15% weight aqueous dispersion, AQUACOAT® or SURELEASE®) is plasticized with triethylcitrate (TEC, 20% wt of dry polymer in the Eudragit) for 1–24 h. Talc (50% weight of dry polymer in the Eudragit) is added with mixing

to form the mixture. The rapid-release granules are coated with this mixture until a 10–15% weight increase in granule weight is achieved. The coated granules are then coated with a Eudragit S100 dispersion as done immediately above until a 10–15% weight increase in granule weight is achieved.

9. Sustained-Release Granules: This procedure employs a double granulation. Thus, DFMO (500 g), MCC (500 g), and Eudragit RS 30D (75–100 g) are mixed. To this mixture is added sufficient water to yield a 30% weight suspension. To the suspension is added TEC (10% weight based on dry polymer weight of Eudragit) to yield a dispersion that is wet granulated and dried to remove as much water as possible. The granules are then ground into a fine powder. To the powder is added sufficient water to make a wet mass that is extruded, spheronized, dried, ground, and screened (size 14–20 mesh).
10. Gastric-, Enteric-, and Colorectal-Release Granules: The following procedure details the preparation of the dosage form. Rapid gastric-release granules (450 g, prepared previously), rapid enteric-release granules (100 g, prepared previously), and slow colorectal-release granules (450 g, prepared previously) are mixed thoroughly. Hard gelatin capsules are then filled with the mixture.

Diltiazem Hydrochloride Extended-Release Capsules

Diltiazem hydrochloride is a calcium ion cellular influx inhibitor (slow channel blocker). The extended-release capsules contain diltiazem hydrochloride in extended-release beads at doses of 120, 180, 240, 300, 360, and 420 mg. They also contains: microcrystalline cellulose, sucrose stearate, Eudragit, povidone, talc, magnesium stearate, hydroxypropyl methylcellulose, titanium dioxide, polysorbate, simethicone, gelatin, FD&C Blue No. 1, FD&C Red No. 40, D&C Red No. 28, FD&C Green No, 3, black iron oxide, and other solids.

In another formulation, the 120 mg, 180 mg, 240 mg, and 300 mg capsules also contain: black iron oxide, ethylcellulose, FD&C Blue No. 1, fumaric acid, gelatin, sucrose, starch, talc, titanium dioxide, white wax, and other ingredients. The 360 mg capsule also contains: black iron oxide, diethyl phthalate, FD&C Blue No. 1, gelatin, povidone K17, sodium lauryl sulfate, starch, sucrose, talc, titanium dioxide, and other ingredients.

The rapid-release pellets of diltiazem can be manufactured by the following procedure: 2.00 kg of microgranules composed of sucrose and starch, with a particle size of 0.500–0.710 mm, are rotated in a trough with a stainless steel basket that is 450 mm in diameter. The rotating mass is sprayed, by means of a membrane-type proportioning pump, with 26 g of a 40% strength solution of shellac in ethanol and sprinkled with 80 g of diltiazem with a particle size of 40–80 μm.

MANUFACTURING DIRECTIONS

The sustained release pellets can be manufactured by following procedure: 2.00 kg of saccharose/starch pellets having a particle size between 0.500 and 0.710 mm are put in rotation in a suitable coating pan. The rotating mass is sprayed with 27.2 g of an ethanolic solution containing 9.79 g of shellac and 1.09 g of polyvinylpyrrolidone; and 80 g of diltiazem HCl are added. This operation is repeated 50 times. These pellets are then coated with the same amount of solution of ethylcellulose N100 and talc, respectively, 80 g of 0.5% solution of ethylcellulose N100, and 54 g of talc. This operation is repeated 25 times. The proportion of soluble vs. insoluble coating materials can be altered to obtain the best release profile. All the formulations are tested for *in vitro* dissolution, in the range of pH between 1 and 7.5, using the method described in the USP, paddle apparatus.

Alternate methods of preparing coated beads include first preparing beads and then coating them; the plain beads are prepared by:

FORMULA 1

Diltiazem hydrochloride	1120.00 g
Lactose	119.00 g
Microcrystalline cellulose (Avicel pH101)	140.00 g
Povidone K30	21.00 g

After introducing the powders into a planetary mixer and granulating same through the obtained plastic, mass is extruded through a cylinder with 1 mm diameter holes (Alexanderwork). The small cylinders are rounded, so as to obtain beads, by means of a spheronizer. After drying at 60°C for 12 h, the beads are sifted and the fraction with size comprised between 0.7 mm and 1.4 mm are retained. 1,179 g of beads were obtained yield (84%).

FORMULA 2

Diltiazem HCl	560.00 g
Crodesta F 160	59.50 g
Microcrystalline cellulose (Avicel pH101)	70.00 g
Povidone K30	10.50 g

The ingredients are introduced in a planetary mixer and dry mixed for approximately 15 min. Thereafter, 100 ml purified water is added, and the mixing is pursued for 10 min more until a plastic mass is obtained. This mass is then extruded through a Fuji Paudal® extruder equipped with a 1-mm screen to obtain "spaghetti." A spheronizer-type caleva is used to transform the extruded product into beads. After drying for 12 h on trays in an oven at 60°C, the beads are sieved to eliminate the ones with a size larger than 1.4 mm and with a size smaller than 0.7 mm. The amount of beads obtained with sizes between 0.7 mm and 1.4 mm was 639.1 g (yield 91.3%).

The beads prepared previously are then coated in a STREA-1 (Aeromatic®) fluidized bed using the "top spraying" technique, and 440 g of coating suspension from the following composition is applied on 500 g of beads. Thereafter, the coated beads are dried at 50°C for 16 h.

COATING SUSPENSION COMPOSITION

Magnesium stearate	12.50 g
Titanium dioxide	5.00 g
Povidone K30	5.00 g
Eudragit NE30D	620.00 g
Talc	17.50 g
Water	338.00 g
Simethicone	1.00 g
Tween 80	0.80 g

Diphenhydramine Hydrochloride Capsules

Each capsule contains diphenhydramine hydrochloride 25 mg. Each capsule contains: lactose and magnesium stearate. The banded capsule shell contains: D&C Red No. 28, FD&C Red No. 3, FD&C Red No. 40, FD&C Blue No. 1, gelatin, glyceryl monooleate, and titanium dioxide.

Dipyridamole and Aspirin Extended-Release Capsules

This is a combination antiplatelet agent intended for oral administration. Each hard gelatin capsule contains 200 mg of dipyridamole in an extended-release form and 25 mg of aspirin as an immediate-release sugar-coated tablet. In addition, each capsule contains the following inactive ingredients: acacia, aluminum stearate, colloidal silicon dioxide, cornstarch, dimethicone, hydroxypropyl methylcellulose, hydroxypropyl methylcellulose phthalate, lactose monohydrate, methacrylic acid copolymer, microcrystalline cellulose, povidone, stearic acid, sucrose, talc, tartaric acid, titanium dioxide, and triacetin. Each capsule shell contains gelatin, red iron oxide and yellow iron oxide, titanium dioxide, and water. Dipyridamole is an antiplatelet agent chemically described as 2,6-bis(diethanolamino)-4,8-dipiperidino-pyrimido(5,4-d) pyrimidine (= dipyridamole). The antiplatelet agent aspirin (acetylsalicylic acid) is chemically known as benzoic acid, 2-(acetyloxy).

Divalproex Sodium Capsules

Divalproex sodium is a stable coordination compound comprised of sodium valproate and valproic acid in a 1:1 molar relationship and formed during the partial neutralization of valproic acid with 0.5 equivalent of sodium hydroxide. Chemically, it is designated as sodium hydrogen *bis* (2-propylpentanoate). The sprinkle capsules are for oral administration and contain specially coated particles of divalproex sodium equivalent to 125 mg of valproic acid in a hard gelatin capsule. The inactive ingredients in the 125-mg sprinkle capsules are: cellulosic polymers, D&C Red No. 28, FD&C Blue No. 1, gelatin, iron oxide, magnesium stearate, silica gel, titanium dioxide, and triethyl citrate.

Divalproex Sodium Coated Particle Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
125.00	1	Valproic Acid, USE Divalproex Sodium Coated Particles	134.50
0.53	2	Magnesium Stearate	0.53
1.00	3	Silica Gel (Syloid 244)	1.00

MANUFACTURING DIRECTIONS

1. Prepare coated particles of divalproex sodium by coating with ethylcellulose (34.34 mg), triethyl citrate (5.8 mg), and magnesium citrate (35 mg), using a mixture of alcohol and acetone in an air suspension system; screen particles using 20- and 40-mesh screens; particles larger than 20 and smaller than 40 must be reworked.
2. Make the granules by wet granulation of divalproex sodium and silica gel, using alcohol.
3. Collect 20–40 mesh granules after drying not more than 50°C to loss on drying of not more than 0.5%.

Dofetilide Capsules

Dofetilide is an antiarrhythmic drug with Class III (cardiac action potential duration prolonging) properties. Each capsule contains the following inactive ingredients: microcrystalline cellulose, cornstarch, colloidal silicon dioxide, and magnesium stearate. It is supplied for oral administration in three dosage strengths: 125 mcg (0.125 mg) orange and white capsules; 250 mcg (0.25 mg) peach capsules; and 500 mcg (0.5 mg) peach and white capsules.

Doxepin Hydrochloride Capsules

Doxepin hydrochloride is one of a class of psychotherapeutic agents known as dibenzoxepin tricyclic compounds. It is a white crystalline solid that is readily soluble in water, lower alcohols, and chloroform. Inert ingredients for the capsule formulations are: hard gelatin capsules (which may contain Blue 1, Red 3, Red 40, Yellow 10, and other inert ingredients); magnesium stearate; sodium lauryl sulfate; and starch.

Doxycycline Capsules

Doxycycline is a broad-spectrum antibiotic synthetically derived from oxytetracycline. Available as 100 mg and 50 mg capsules, they contain doxycycline monohydrate equivalent to 100 mg or 50 mg of doxycycline for oral administration. The inert ingredients are: colloidal silicon dioxide; magnesium stearate; microcrystalline cellulose; and sodium starch glycolate.

Doxycycline Hyclate Capsules

These capsules contain specially coated pellets of doxycycline hyclate for oral administration. They also contain lactose, microcrystalline cellulose, and povidone. The capsule shell and band contain FD&C Blue No. 1, FD&C Yellow No. 6, D&C Yellow No. 10, gelatin, silicon dioxide, sodium lauryl sulfate, and titanium dioxide. Doxycycline is a broad-spectrum antibiotic that is synthetically derived from oxytetracycline and is available as doxycycline hyclate. The chemical designation of this light-yellow crystalline powder is alpha-6-desoxy-5-oxytetracycline. Doxycycline has a high degree of lipid solubility and a low affinity for calcium binding. It is highly stable in normal human serum. Doxycycline will not degrade into an epianhydro form.

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
122.00	1	Doxycycline Hyclate (22% excess)	122.00
26.00	2	Microcrystalline Cellulose (Avicel PH 102)	26.00
4.00	3	Starch (Cornstarch Dried)	4.00
0.60	4	Sodium Lauryl Sulfate	0.60
0.60	5	Colloidal Silicon Dioxide (Aerosil 200)	0.60
2.00	6	Magnesium Stearate	2.00
—	7	Hard Gelatin Capsules, Size 3	1000.00

MANUFACTURING DIRECTIONS

Note: Processing should be conducted in a controlled room temperature and humidity area. The limits are: room temperature 20–27°C; RH 40–45%.

1. Mix Items 1, 2, and 4 in a stainless steel drum. Pass the mixed material through a 500-µm sieve using a sifter. Collect in stainless steel drum.
2. Mix Items 3, 5, and 6 in a polyethylene bag. Pass the mixed material through a 250-µm sieve using a sifter. Pass two times. Collect in the polyethylene bag, and transfer to Step 1 in a stainless steel drum.
3. Mix the material in a drum mixer for 3 min.
4. Take a sample for assay and moisture content.
5. Load the empty capsule shells (size 3) in the hopper; cap is ivory opaque, and body is ivory opaque.
6. Run the machine, and check the locking of shells. Run the machine. Check the fill weight (155 mg) and locking of the capsules. Collect the filled capsules, from polyethylene-lined stainless steel container, in silica bags and close tightly.
7. Store the containers in a controlled room temperature and humidity area. The limits are: RH 45–50% at a temperature of 25–27°C.

Doxycycline Hydrochloride Capsules and Oral Suspension

It is a broad-spectrum antibiotic that is synthetically derived from oxytetracycline. The chemical designation for doxycycline is 4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide monohydrate. Inert ingredients in the capsule formulations are: hard gelatin capsules (which may contain Blue 1 and other inert ingredients); magnesium stearate; microcrystalline cellulose; and sodium lauryl sulfate. Inert ingredients for the oral suspension formulation are: carboxymethylcellulose sodium; Blue 1; methylparaben; microcrystalline cellulose; propylparaben; raspberry flavor; Red 28; and simethicone.

Efavirenz Capsules

Efavirenz is an HIV-1 specific, non-nucleoside, reverse transcriptase inhibitor (NNRTI). Efavirenz is chemically described as (S)-6-chloro-4-(cyclopropylethynyl)-1,4-dihydro-4-(trifluoromethyl)-2H-3,1-benzoxazin-2-one. It is available as capsules for oral administration containing either 50 mg, 100 mg, or 200 mg of efavirenz as well as the following inactive ingredients: lactose monohydrate, magnesium stearate, sodium lauryl sulfate, and sodium starch glycolate. The capsule shell contains the following inactive ingredients and dyes: gelatin, sodium lauryl sulfate, titanium dioxide, and yellow iron oxide. The capsule shells may also contain silicon dioxide. The capsules are printed with ink containing carmine 40 blue, FD&C Blue No. 2, and titanium dioxide.

Enalapril Maleate Capsules

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
10.00	1	Enalapril Maleate	10.00
235.00	2	Lactose Anhydrous	235.00
1.25	3	Magnesium Stearate	1.25

MANUFACTURING DIRECTIONS

1. Pass all items through No. 60 mesh into blender; mix for 10 min.
2. Fill 250 mg.

Erythromycin and Bromhexine Powder for Suspension

Bill of Materials			
Scale (mg/5 ml)	**Item**	**Material Name**	**Qty/l (g)**
21.00	1	Sodium Carboxymethylcellulose	0.42
6.55	2	Dye Red	0.131
4735.00	3	Sugar Granular 39075 Mesh	94.70
2650.00	4	Sodium Citrate Dihydrate	53.00
659.00	5	Sodium Carboxymethylcellulose High Viscosity	13.18
393.50	6	Magnesium Aluminum Silicate Veegum F	7.87
78.50	7	Saccharin Sodium Dihydrate	1.57
200.00	8	Erythromycin, USE Erythromycin Ethylsuccinate[a] Citrate Washed	123.58
0.80	9	Bromhexine, USE Bromhexine Hydrochloride	2.10
QS	10	Flavor	3.95
QS	11	Water Purified, ca	67 ml

[a] Erythromycin Ethylsuccinate is factored = (123.58 × 850)/potency, mcg/g.

MANUFACTURING DIRECTIONS

I. Granulation
   A. Dissolve the sodium carboxymethylcellulose (Item 1) and the dye in approximately 67 ml of purified water with heat while stirring. Allow to cool. Ensure that the sodium carboxymethylcellulose is completely in solution.
   B. Pass sugar cane through a 2.38-mm aperture screen using an oscillating granulator.
   C. Pass the following through a 1.27-mm aperture or similar screen: sodium CMC (Item 5), veegum F, sodium saccharin, bromhexine HCl, and erythromycin ethylsuccinate. Use a Fitz mill or a similar mill, high speed, impact forward.
   D. Load the ingredients from Steps B and C into the mixer, and blend for 30 min.
   E. Mass with the solution from Step A. If necessary, add purified water to form a cohesive granule with even color dispersion.
   F. If necessary, pass the wet mass through a 4.76-mm aperture screen, and spread on stainless steel trays.
   G. Load trays of granulation into the oven, and dry at 49°C to loss on drying (LOD) of less than 0.5% (60°C/5 mm).
      Note: Stir granulation during drying.
   H. Allow granulation to cool in low-humidity area before passing through a 1.7-mm aperture screen.
      Note: Pre-cooling in a low-humidity area prevents condensation when later packed in polyethylene-lined bags.
   I. Request samples.
   J. Charge part of dry granulation and sodium citrate into a mixer. Slowly add flavor while mixing. Mix for a few minutes. Hand screen through a 1.2-mm aperture screen.
   K. Charge the screened granulation into a suitable blender, and add flavor mixture from Step J. Mix well (approximately 30 min).
   L. Take samples.
   M. Discharge blended granulation into tared polyethylene-lined drums; seal and weigh. Store until needed for filling.

II. Finishing
   A. At filling, weight for a 60-ml bottle should be 22.85 g; weight for a 100-ml bottle should be 39.08 g.

Erythromycin and Sulfisoxazole Granules for Suspension

Bill of Materials			
Scale (mg/5 ml)	**Item**	**Material Name**	**Qty/kg (g)**
180.63	1	Sodium Citrate Dihydrate	66.90
600.00	2	Sulfisoxazole, USE Sulfisoxazole Acetyl	222.30
13.50	3	Sodium Carboxymethylcellulose High Viscosity	5.00
10.80	4	Magnesium Aluminum Silicate Veegum F	4.00
5.40	5	Citric Acid	2.00
0.54	6	Polaxamer 188 (Pluronic F68)	0.20
200.00	7	Erythromycin, USE Erythromycin Ethylsuccinate Citrate Washed[a] (850 mcg/mg) 5% Excess	75.29
1661.28	8	Sucrose	615.29
QS	9	Water Purified	55 ml
7.56	10	Flavor	2.80
3.24	11	Flavor	1.20
10.80	12	Flavor	4.00
2.70	13	Ammonium Glycyrrhizinate	1.00

[a] Factored according to potency. Adjust with sugar.

MANUFACTURING DIRECTIONS

I. Premixing
Note: This milling step is hazardous.
CAUTION: EQUIPMENT MUST BE GROUNDED OR BONDED.
   A. Mill sodium citrate, sodium carboxymethylcellulose, magnesium aluminum silicate, citric acid. poloxamer and erythromycin ethylsuccinate through a no. 2 band (1.59-mm aperture) using a Fitz mill or similar mill, at high speed, impact forward.
   B. Load milled materials from Step A into a suitable blender. Mix for 15 min.
   C. Screen the sulfisoxazole acetyl through a 4.76-mm aperture screen, and add to the blender. Blend for 15 min.
   D. Discharge blender into polyethylene-lined drums.

II. Granulation
   A. Load mass mixer with the premix blend. Add the sucrose to mixer by hand screening through a 2.00-mm aperture screen. Dry mix for not less than 5 min.
   B. QS to mass using approximately 51 ml of purified water.
   C. Granulate the wet mass through a 5/8-in. band (15.88-mm aperture or similar) on a rotary granulator or similar granulator. Spread on paper-lined trays, no more than one scoopful per tray. Place granulation in oven set at 49°C.
   D. Dry to not more than a 0.7% loss on drying.
   E. Sift dried granulation through a 1.19-mm aperture screen, and grind coarse granulation through a no. 2AA band (1.98-mm aperture or similar) in a Fitz mill or a similar mill, medium speed, knives forward into polyethylene-lined drums.

III. Blending
   A. Load approximately one-half of the granulation from Step II-E into a suitable blender.
   B. Screen flavors and ammonium glycyrrhizinate through a 600-µm aperture screen into a portion of the granulation; mix and add to the blender.
   C. Add the remaining granulation into the blender. Blend for 20 min.
   D. Discharge mixture into polyethylene-lined drums.

IV. Finishing
   A. Fill into suitable approved bottles at a theoretical weight of 62.5 g per 100 ml, requiring approximately 50 ml of water for reconstitution.

Erythromycin Delayed-Release Capsules

Erythromycin delayed-release capsules contain enteric-coated pellets of erythromycin base for oral administration. Erythromycin is produced by a strain of *Streptomyces erythraeus* and belongs to the macrolide group of antibiotics. It is basic and readily forms salts with acids, but it is the base that is microbiologically active. Each erythromycin delayed-release capsule contains 250 mg of erythromycin base. The inactive ingredients are: cellulosic polymers, citrate ester, D&C Red No. 30, D&C Yellow No. 10, magnesium stearate, and povidone. The capsule shell contains FD&C Blue No. 1, FD&C Red No. 3, gelatin, and titanium dioxide.

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
250.00	1	Erythromycin, USE Erythromycin 66.7% Pellets (label claim is 667 mg/gm)	375.00[a]
—	2	Empty Hard Gelatin Capsule, Size 0	1000

[a] Quantity of pellets for 1000 capsules will be adjusted based on the pellets assay results.

MANUFACTURING DIRECTIONS

Note: Processing should be done under controlled room temperature and relative humidity. The limits are: room temperature 20–25°C; RH 40–45%.

1. Load the empty capsule shells (size 0), in the hopper.
2. Fill.

Erythromycin Ethylsuccinate for Oral Suspension

Bill of Materials			
Scale (mg/5 ml)	**Item**	**Material Name**	**Qty/1 kg (19 units) (g)**
125.00	1	Erythromycin Ethylsuccinate[a]	55.860
2168.00	2	Sucrose[b]	823.840
250.25	3	Sodium Citrate	95.095
2.97	4	Saccharin Sodium	1.128
0.27	5	FD&C Red No. 40	0.104
1.43	6	Carmellose Sodium (Sodium CMC 7 MFD)	0.543
21.45	7	Simethicone Emulsion 30% (Simethicone M30)	8.151
12.98	8	Xanthan Gum	4.932
6.27	9	Cherry Dry Flavor	2.382
—	10	Purified Water	15.200

[a] Potency: 850 mcg/mg, as is.
[b] Sucrose quantity to be adjusted accordingly. The weight of sucrose may be adjusted to compensate for potency variation of erythromycin ethylsuccinate to maintain the standard batch size (1 kg). Fill weight: 52.5 gm for 100-ml pack.

MANUFACTURING DIRECTIONS

Precautions: Handle erythromycin ethylsuccinate carefully to avoid any cross contamination. The processing area must be under controlled room temperature and humidity. The limits are: RH: 45–55%; temperature: 23–25°C.

1. Preparation of Solution: Dissolve Item 5 in Item 10 (25–30°C). Add Item 6 slowly while stirring with stirrer at medium speed until gel is formed. Check the weight; theoretical weight is 15.84 g. If required, adjust with Item 10.
2. Dry Mixing: Pass Item 2 (calculated quantity) through sifter using a 900-µm sieve. Crush the larger crystals of Item 2 using a Fitz mill, impact forward, high speed.
3. Load Item 2 from Step 2 into the mixer, and start mixing at high speed. Add Item 7 while mixing. Mix for 10 min with the mixer and chopper at high speed.
4. Mix Items 3, 4, 8, 1, and the mixture from Step 3 in a clean, dry stainless steel container using a clean, dry stainless steel scoop.
5. Pass the material through a Fitz mill, impact forward, high speed.
6. Add the milled material to the mixer; mix for 5 min with the mixer and chopper at high speed.
7. Scrap down the sides and blades and again mix for 2 min with the mixer and chopper at high speed.
8. Wet Granulation: Very slowly add the solution from Step 1 to Step 5 in mixer. Mix at low speed, until a satisfactory mass is obtained. Mix and chop for 1 min only. Do not over wet the mass.
9. Drying: Dry the wet granules in the fluid-bed dryer at 55°C to reach a loss on drying of no more than 0.4%.
10. Grinding: Pass the dried granules through a 1.0-mm sieve using Frewitt® granulator. Collect in a stainless steel drum.
11. Final Mixing: Pass Item 9 through 250-µm sieve using a sifter. Collect in a polyethylene-lined bag.
12 Load sieved material from Step 8 into the blender.
13. Add sieved flavor (Item 9) from Step 11 to the blender.
14. Blend the powders for 5 min.
15. Unload the blended powder in stainless steel drums.

Erythromycin Ethylsuccinate for Oral Suspension 200 mg/5 ml

Bill of Materials			
Scale (mg/5 ml)	**Item**	**Material Name**	**Qty/1 kg (18 Units) (g)**
200.00	1	Erythromycin, USE Erythromycin Ethylsuccinate[a]	89.3700
1342.00	2	Sucrose	483.1200
880.00	3	Sucrose[b]	316.8000
250.25	4	Sodium Citrate	90.0900
2.97	5	Saccharin Sodium	1.0692
0.27	6	FD&C Red No. 40	0.0990
1.43	7	Carmellose Sodium (Sodium CMC 7 MFD)	0.5148
21.45	8	Simethicone Emulsion 30% (Simethicone M30)	7.7220
12.98	9	Xanthan Gum	4.6728
6.27	10	Cherry Dry Flavor	2.2572
—	11	Purified Water	15.8400

[a] Potency: 850 mcg/mg, as is.
[b] The weight of sucrose may be adjusted to compensate for potency variation of erythromycin ethylsuccinate to maintain the standard batch size (1 kg). Fill Weight: 55 gm for 100-ml pack.

Erythromycin Stearate for Oral Suspension

1.

Bill of Materials			
Scale (mg/ml)	**Item**	**Material Name**	**Qty/l (g)**
25.00	1	Erythromycin Stearate 600 mcg/mg, 5% excess	43.75
1.00	2	Methyl Paraben	1.00
0.20	3	Propyl Paraben	0.20
10.00	4	Magnesium Aluminum Silicate	10.00
1.15	5	Sodium Carboxymethylcellulose (CMC), low viscosity	1.15
4.00	6	Alcohol 190 Proof	4.00
120.00	7	Sodium Citrate Dihydrate	120.00
0.20	8	Saccharin Sodium	0.20
700.00	9	Sugar Granular	700.00
0.07	10	Yellow Dye	0.07
2.76	11	Chocolate Flavor	2.76
0.54	12	Orange Flavor	0.54
1.25	13	Sodium Lauryl Sulfate	1.25
QS	14	Water Purified	QS

MANUFACTURING DIRECTIONS

I. Mixing
   A. Place sodium CMC and 40 g of sugar in a mixing drum. (If using alcohol, add it to the drum to wet the mixture, and indicate use on the work order.) Roll for 2 h to blend.
   B. Measure 350 ml of purified water into a jacketed mixing tank, and heat the water to 95°C. Maintain at this temperature.
   C. Add methyl paraben to the water at 95°C. Stir until completely dissolved.
   D. Add propyl paraben to the solution at 95°C. Stir until completely dissolved.
   E. Cool to 60°C and maintain temperature. Stir the solution and slowly sprinkle in Veegum®. Stir until veegum is completely dispersed. Check by passing quantity of the batch through a 350-µm aperture or similar screen, and watch for any undissolved residue.
   F. While stirring, add the blended powders from Step A slowly to the solution. Stir until completely dissolved. Screen a quantity through a 350-µm aperture or similar screen to check for undissolved sodium CMC.
   G. Maintain the batch at 50–55°C, and gradually add the remaining sugar (Item 9) with stirring. Stir until completely dissolved. Check for any undissolved sugar by passing a quantity of the bulk through a 350-µm aperture or similar screen.
   H. Dissolve the saccharin sodium in approximately 5 ml of purified water, and add the solution to the batch.
   I. While stirring, add the sodium citrate to the batch. Stir under maximum vacuum until completely dissolved. Check by passing a quantity of the bulk through a 350-µm aperture or similar screen.
   J. Dissolve FD&C Yellow No. 6 in approximately 5 ml of purified water, and add the solution to the batch. Cool the batch to 30°C (chilled water may be used).
   K. In a separate tank, stir approximately 85 ml of purified water and slowly, taking care to avoid a vortex, add and dissolve sodium lauryl sulfate. When dissolved, gradually sprinkle in the erythromycin stearate, and mix into a smooth slurry. Mix for 1/2 h.
   L. While stirring the batch from Step J, slowly add the slurry from Step K. Take care not to aerate the batch. Wash thoroughly into the batch with approximately 10 ml of purified water.
   M. With continual stirring, add the flavors (Items 11 and 12) to the batch.
   N. Pass the whole batch through a homogenizing mill, using a suitable setting such that crystal fracture is minimized. Rinse the mill with purified water, and add the rinsings to the batch.
   O. Return the milled batch back into the mixing tank. Gradually increase the application of

vacuum as allowed by the level in the tank. Stir under a 28-in. Hg vacuum for 1 h. Adjust the batch volume to 1 l, using purified water.

P. Repeat Step O until the volume is constant and specific gravity meets specifications.

2.

Bill of Materials			
Scale (mg/ml)	**Item**	**Material Name**	**Qty/l (g)**
25.00	1	Erythromycin Stearate 600 mcg/mg, 5% excess	43.75
1.00	2	Methyl Paraben	1.00
0.20	3	Propyl Paraben	0.20
2.00	4	Xanthan Gum	2.00
120.00	5	Sodium Citrate Dihydrate	120.00
0.20	6	Saccharin Sodium	0.20
100.00	7	Sorbitol Solution	100.00
4.50	8	Antifoam Emulsion Dow Corning	4.50
0.07	9	Dye Yellow	0.07
2.76	10	Flavor Chocolate	2.76
700.00	11	Sugar Granular	700.00
0.54	12	Flavor Orange	0.54
1.25	13	Sodium Lauryl Sulfate	1.25
QS	14	Water Purified	QS

MANUFACTURING DIRECTIONS

I. Mixing
   A. Heat 600 ml of purified water in a jacketed mixing tank to 95–100°C.
   B. Add the methyl paraben and propyl paraben and mix to dissolve.
   C. Withdraw the following preserved purified water:
      1. 200 ml and dissolve the sodium citrate.
      2. 150 ml and dissolve the sodium lauryl sulfate.
      3. 5 ml and dissolve the sodium saccharin and the dye yellow.
   D. In a plastic bag, mix together the xanthan gum and 20 g of sucrose (Item 11) for 10 min.
   E. Maintaining the batch at 50–60°C while mixing, slowly add the dry mixture from Step D, until a clear gel is obtained.
   F. Add the sorbitol and mix.
   G. While mixing, slowly add the solution obtained from Step C-1.
   H. Add the disperse 380 g of sucrose (Item 11) while mixing. Make sure that the temperature will not go over 60°C. Stop heating when all dissolved.
   I. Without producing the vortex, add erythromycin stearate to the solution from Step C-2, and continue mixing until smooth slurry is formed. Continue mixing for 15–30 min, and then pass slurry through a homogenizer. Add the Antifoam C to the slurry and mix; rinse the homogenizer with purified water, and add the rinsings to the slurry. Mix.
   J. While mixing, add the slurry obtained from Step I to the batch; rinse the vessel with 5 ml of purified water, and add the rinsings to the batch.
   K. Add and disperse the solution from Step C-3, and continue mixing.
   L. Mix under vacuum for 1 h. Release the vacuum and record the volume.
      CAUTION: DO NOT ADJUST VOLUME AT THIS STAGE.
   M. Repeat Step L until no further volume change is noticed.
   N. Add the flavors (Items 10 and 11) and bring to volume with purified water.

Erythropoietin Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
14,000 IU	1	Erythropoietin[a]	140,000,000 IU
0.047	2	Dimyristoyl Phosphatidyl Choline	0.047
3.42	3	Aprotinin[b]	3.42
3.78	4	Hydroxypropyl Cellulose-LF	3.78
3.78	5	Polyoxy-40 Stearate Myrj-52®	3.78
141.1	6	Polyethylene Glycol 400	141.1
15.72	7	Propylene Glycol	15.72
8.83	8	Phosphate Buffer	8.83
31.49	9	Cholesterol	31.49
17.72	10	Tween 80	17.72
63.68	11	Egg Yolk Lecithin	63.68
28.15	12	Glyceryl Amino Oleate	28.15
19.78	13	d-alpha Tocopherol	19.78
251.42	14	Oleic Acid	251.42

[a] Erythropoietin: 1000 IU = 8 μg.
[b] Aprotinin: 7500 KIU = 1.0 mg.

MANUFACTURING DIRECTIONS

1. Erythropoietin is a 165 amino acid glycoprotein of approximately 34,000 daltons. It is an endogenous protein, which is involved in the production of red blood cells. It is indicated for the treatment of anemia associated with chronic renal failure, in AIDS patients, and also to maintain or elevate the red blood cell level in the human body. In its preparations, there can be no use of heat or alcohol that can denature it.
2. The overall method is as follows: The high HLB surfactant polyoxy-40 stearate is slowly dispersed into the mixture of polyethylene glycol 400 and propylene glycol. Once it dissolves, hydroxypropyl cellulose as a stabilizer is also added which is dispersed slowly into the above mixture. A separate solution of the proteinaceous material along with the phospholipid and the protease inhibitor is made in a portion of the above solvent mixture. The solution can then be added to the PEG/PG mixture at room temperature. The amount of any water is limited to 5% of the polyol solvent. When the water solution is used, citrate buffer is used to maintain the pH at a point where the protein is most stable. For erythropoietin, pH can be adjusted to 7.0–7.5 with a phosphate buffer. The amount of aqueous buffer solution would still be 5% of the hydrophilic phase. At a pH of 7.0–7.5, erythropoietin has its maximum stability. It is known that in formulating proteins, the pH of the formulation should be distant from the isoelectric point of the protein which would not precipitate the protein from the solution. Separately, the ingredients of the lipid solvent are mixed together. Under gentle and constant stirring, the polyol solution is dispersed with the lipid solution.
3. The surfactant (polyoxy-40 stearate) is slowly dispersed into a mixture of polyethylene glycol and propylene glycol. Once it is dissolved, small amounts of hydroxypropyl cellulose are then added and dispersed into the same mixture. Erythropoietin is dissolved in the phosphate buffer/water/saline, along with aprotinin and dimyristoyl phosphatidyl choline. The aqueous solution is then added to the polyethylene glycol mixture at room temperature. The pH of the solution should be adjusted at 7.5 for maximum stability.
4. In a separate vessel, dissolve all the lipid-liking ingredients in oleic acid. Cholesterol is added slowly to achieve faster dissolution. Once both the phases are ready, the lipid solution is added slowly to polyol solution while mixing at low speed. Preferably, the vessel should be ice jacketed because mixing produces heat. Once the mixing is achieved, a transparent yellowish-brown preemulsion solution is obtained.
5. The preemulsion solution is filled in a size 0 hard gelatin capsule, and the capsule is sealed

with a band of gelatin solution. The banding helps to coat the capsule uniformly.

6. The capsule is then coated with a 10% hydroxypropyl methylcellulose solution as an undercoat. The amount of coat required is sufficient just enough to cover the capsule uniformly with a thin layer of the polymer coat. Usually, a 3.5–4.5% weight gain of the capsule is a good indication of the amount required as an undercoat.
7. Once the capsule is coated with an undercoat, enteric coating is applied. For enteric coating purposes, different polymers, such as hydroxypropyl methylcellulose, hydroxypropyl methylcellulose phthalate, and cellulose acetate phthalate, are used.
8. Anionic copolymers that are based on methacrylic acid and methyl methycrate, commercially available as Eudragit, are also very suitable polymers for enteric coating purposes. The polymer is dissolved in organic solvents such as ethyl alcohol, methyl alcohol, acetone, isopropyl alcohol. A combination of two solvents can also be used. The amount of enteric coating solution required is 5–6% of the weight gain of the capsules from the original weight of the capsules before applying an enteric coat.

A typical enteric coating solution is made as follows:

Methacrylic acid and Methycrate copolymer 10% w/w
Diethyl butyl phthalate (plasticizer) 2% w/w
Acetone 22% w/w
Isopropanol 66% w/w

Procedure: Mix acetone and isopropanol. Add the polymer slowly with constant mixing. Once the polymer is dissolved, add the plasticizer slowly and let it dissolve.

For a size 0 capsule, the previously mentioned enteric coating solution can be sprayed using fluidizing bed techniques. The fluid bed sprayer/dryer is operated with the following parameters:

Flow rate: 1.5 ml/minute
Inlet air temperature: 25°C
Outlet air temperature: 25°C
Air flap: 35
Atomizer: 2.0 bar
A size 0 capsule after the enteric coating will typically have the following composition:
Preemulsion solution: 0.589 g
Undercoat polymer: 0.027 g
Enteric coat polymer: 0.032 g, 0.648 g

Esomeprazole Magnesium Capsules

The active ingredient, esomeprazole magnesium, in delayed-release capsules is bis(5-methoxy-2-[(S)-[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1 *H*-benzimidazole-1-yl) magnesium trihydrate, a compound that inhibits gastric acid secretion. Esomeprazole is the S-isomer of omeprazole, which is a mixture of the S- and R-isomers. Each delayed-release capsule contains 20 mg or 40 mg of esomeprazole (present as 22.3 mg or 44.5 mg esomeprazole magnesium trihydrate) in the form of enteric-coated pellets with the following inactive ingredients: glyceryl monostearate 40-50, hydroxypropyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, methacrylic acid copolymer type C, polysorbate 80, sugar spheres, talc, and triethyl citrate. The capsule shells have the following inactive ingredients: gelatin, FD&C Blue No. 1, FD&C Red No. 40, D&C Red No. 28, titanium dioxide, shellac, ethyl alcohol, isopropyl alcohol, n-butyl alcohol, propylene glycol, sodium hydroxide, polyvinyl pyrrolidone, and D&C Yellow No. 10.

Estramustine Phosphate Capsules

Estramustine phosphate sodium is an antineoplastic agent. The capsules are white and opaque, each containing estramustine phosphate sodium as the disodium salt monohydrate that is equivalent to 140 mg estramustine phosphate, for oral administration. Each capsule also contains magnesium stearate, silicon dioxide, sodium lauryl sulfate, and talc. Gelatin capsule shells contain titanium dioxide.

Ethosuximide Capsules

Ethosuximide is an anticonvulsant succinimide that is chemically designated as alpha-ethyl-alpha-methyl-succinimide. Each capsule contains 250 mg ethosuximide, and the inactive ingredient polyethylene glycol. The capsule contains D&C Yellow No. 10; FD&C Red No. 3; gelatin, glycerin, and sorbitol.

Etodolac Capsules

Etodolac is a pyranocarboxylic acid. The inactive ingredients in the capsules are: cellulose, gelatin, iron oxides, lactose, magnesium stearate, povidone, sodium lauryl sulfate, sodium starch glycolate, and titanium dioxide.

Eye Nutrition Supplement Capsules

This is an antioxidant supplement formulated to provide nutritional support for the eye. It contains essential antioxidant vitamins, minerals, and 6 mg of lutein. Each capsule contains: ascorbic acid, 60 mg; dl-alpha tocopheryl acetate, 30 IU; zinc oxide, 15 mg (elemental); cupric oxide, 2 mg (elemental). The inactive ingredients are: lactose monohydrate, crospovidone, magnesium stearate, and silicone dioxide.

Felbamate for Oral Suspension

Felbamate is an antiepileptic available as a 600 mg/5 ml suspension for oral administration. Its chemical name is 2-phenyl-1,3-propanediol dicarbamate. The inactive ingredients for a felbamate suspension (600 mg/5 ml) are: sorbitol, glycerin, microcrystalline cellulose, carboxymethylcellulose sodium, simethicone, polysorbate 80, methylparaben, saccharin sodium, propylparaben, FD&C Yellow No. 6, FD&C Red No. 40, flavorings, and purified water.

Fenofibrate Capsules

Micronized fenofibrate is a lipid-regulating agent available in capsule form for oral administration. Each capsule contains 67 mg, 134 mg, or 200 mg of micronized fenofibrate. The chemical name for fenofibrate is 2-[4-(4-chlorobenzoyl)phenoxy]-2-methyl-propanoic acid,1-methylethyl ester. Each capsule also contains the following inactive ingredients: crospovidone, iron oxide, lactose, magnesium stearate, pregelatinized starch, sodium lauryl sulfate, and titanium dioxide.

Bill of Materials

Scale(mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
100.00	1	Fenofibrate Micronized (5 µm)	100.00
2.00	2	Sodium Lauryl Sulfate	2.00
100.00	3	Polyvinylpyrrolidone K 25, 100–400 µm	100.00
QS	4	Water Purified	1750.00
114.28	5	Lactose Monohydrate, 100–400 µm	114.28

Note: This formulation is expected to provide enhanced bioavailability of Item 1, thus the dose may be reduced by 33% for all strengths.

MANUFACTURING DIRECTIONS

1. Examine Item 1 using a Coulter® Counter to make sure 90% of particles are within the 5-µm range.
2. Add and dissolve Item 2 in Item 4; Item 1 is then added to make a smooth suspension using a high-speed stirrer and then passing it through a high-speed mill.
3. Add Item 3 while agitating until it is dissolved, and assure that no agglomerates are present.
4. Pass Step 3 through a 350-µm sieve.
5. Separately, Item 5 is charged in a fluid-bed granulator and brought into suspension, and the temperature is raised to 40°C.
6. Add Step 3 into Step 5 gradually at a spraying pressure of 2.1 bar; air throughput of 70 m^3/h; air inlet temperature of 45°C; air outlet temperature of 33°C; product temperature of 34°C; and a spraying duration of 3 h.
7. The granulate thus obtained is filled in a suitable size capsule.

Fexofenadine Hydrochloride Capsules

Fexofenadine hydrochloride is a histamine H1-receptor antagonist with the chemical name (±)-4-[1 hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]-(alpha), (alpha)-dimethyl benzeneacetic acid hydrochloride. It is formulated as a capsule or tablet for oral administration. Each capsule contains 60 mg of fexofenadine hydrochloride and the following excipients: croscarmellose sodium, gelatin, lactose, microcrystalline cellulose, and pregelatinized starch. The printed capsule shell is made from gelatin, iron oxide, silicon dioxide, sodium lauryl sulfate, titanium dioxide, and other ingredients.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
60.00	1	Fexofenadine Hydrochloride[a]	60.00
141.00	2	Microcrystalline Cellulose	141.00
141.00	3	Lactose	141.00
40.00	4	Pregelatinized Starch	40.00
20.00	5	Croscarmellose Sodium	20.00
14.70	6	Gelatin capsules	14.70

[a] Particle surface area of 2–4 m^2/g.

MANUFACTURING DIRECTIONS

1. Combine fexofenadine hydrochloride (Item 1), microcrystalline cellulose (Item 2), lactose (Item 3), and pregelatinized starch (Item 4), and blend in a mixer for 5 min.
2. To this mixture, add a solution of gelatin (Item 6) in purified water (prepared by adding the gelatin to the water and heating the dispersion with mixing until solution of the gelatin is attained), and continue mixing until a good granulation is formed.
3. Pass the granulation through a 0.375-in. screen, and dry at 60°C until a moisture content of less than 3.0% is achieved as determined by a Computrac moisture balance at 125°C.
4. Mill the dried granulation through a 0.065-in. screen.
5. To the granulation, add croscarmellose sodium, and mix for about 10 min.
6. Fill the granulation into size 0 hard gelatin capsules to a total fill weight of 416.7 mg granulation per capsule.

Fluconazole for Oral Suspension

Fluconazole is the first of a new subclass of synthetic triazole antifungal agents. Fluconazole is designated chemically as 2,4-difluoro-(α), 1-bis(1H-1,2,4-triazol-l-ylmethyl) benzyl alcohol. The oral suspension contains 350 mg or 1400 mg of fluconazole and the following inactive ingredients: sucrose, sodium citrate dihydrate, citric acid anhydrous, sodium benzoate, titanium dioxide, colloidal silicon dioxide, xanthan gum, and natural orange flavor. After reconstitution with 24 ml of distilled water or purified water, each ml of reconstituted suspension contains 10 mg or 40 mg of fluconazole.

Flucytosine Capsules

Flucytosine, an antifungal agent, is available as 250-mg and 500-mg capsules for oral administration. Chemically, flucytosine is 5-fluorocytosine, a fluorinated pyrimidine that is related to fluorouracil and floxuridine. Each capsule also contains cornstarch, lactose, and talc. Gelatin capsule shells contain parabens (butyl, methyl, propyl) and sodium propionate, with the following dye systems: 250-mg capsules contain black iron oxide, FD&C Blue No. 1, FD&C Yellow No. 6, D&C Yellow No. 10, and titanium dioxide; 500-mg capsules contain black iron oxide and titanium dioxide.

Fluoxetine Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
20.00	1	Fluoxetine, USE Fluoxetine Hydrochloride	22.36
80.14	2	Starch (Cornstarch)	80.14
10.00	3	Simethicone, USE Simethicone M30	35.00
42.00	4	Starch (Cornstarch Dried)	42.00
0.50	5	Colloidal Silicon Dioxide (Aerosil 200)	0.50
1.00	6	Empty Hard Gelatin Capsule, Shell Size 3	1000.00

MANUFACTURING DIRECTIONS

Note: The processing area must be under controlled room temperature and humidity. The limits are: RH 40–50%; temperature not more than 27°C.

I. Dry powder mixing
   A. Sift Items 1 and 2 through stainless steel sieve (630 μm) in a sifter.
   B. Load the powder mix in the mixer. Mix for 5 min at low speed.

II. Wet massing
   A. Add Item 3 suspension into the powder mix while mixing at low speed for 3 min. Scrape sides and blades. Mix for another 3 min at low speed.

III. Drying and grinding
   A. Spread the moist mass thinly on stainless steel trays. Break the big lumps if any.
   B. Dry the mass in oven at 55°C for 10 h.
   C. Check LOD (limit between 1.5% and 2.0%). If required, dry further for 1 h.
   D. Grind the dried granules through a granulator using a stainless steel sieve (1.00 mm). Collect in a stainless steel drum.

IV. Lubrication
   A. Sift Items 4 and 5 through a stainless steel sieve (500-μm) using a sifter. Collect in a stainless steel drum. Add into the drum blender (Step III-D). Mix for 5 min.
   B. Unload the final blend.

V. Take sample for analyzing fluoxetine hydrochloride content in the granules to fill.
   Note: Encapsulation is recommended within 7 days after lubrication.

Fluoxetine Hydrochloride Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
20.00	1	Fluoxetine, USE Fluoxetine Hydrochloride	22.40
160.00	2	Talc	160.00
100.00	3	Starch Dried	100.00
4.00	4	Magnesium Stearate	4.00
1.00	5	Aerosil 200	1.00

MANUFACTURING DIRECTIONS

1. Charge Items 1–5 in a suitable blender after passing through a No. 60 mesh.
2. Mix for 30 min.
3. Fill 350 mg in size 2 capsules.

Fluoxetine Hydrochloride Instant and Weekly Capsules

Fluoxetine hydrochloride is an antidepressant for oral administration; it is also marketed for the treatment of premenstrual dysphoric disorder. It is chemically unrelated to tricyclic, tetracyclic, or other available antidepressant agents. It is designated N-methyl-3-phenyl-3-[((alpha),(alpha),(alpha)-trifluoro-*p*-tolyl)oxy]propylamine hydrochloride. Each capsule contains fluoxetine hydrochloride equivalent to 10 mg (32.3 μmol), 20 mg (64.7 μmol), or 40 mg (129.3 μmol) of fluoxetine. The Pulvules also contain starch, gelatin, silicone, titanium dioxide, iron oxide, and optionally other inactive ingredients. The 10-mg and 20-mg Pulvules also contain FD&C Blue No. 1, and the 40-mg Pulvule also contains FD&C Blue No. 1 and FD&C Yellow No. 6. The capsules intended for weekly administration, a delayed release formulation, contain enteric-coated pellets of fluoxetine hydrochloride equivalent to 90 mg (291 μmol) of fluoxetine. The capsules also contain FD&C Yellow No. 10, FD&C Blue No. 2, gelatin, hydroxypropyl methylcellulose, hydroxypropyl methylcellulose acetate succinate, sodium lauryl sulfate, sucrose, sugar spheres, talc, titanium dioxide, triethyl citrate, and optionally other inactive ingredients.

Flutamide Capsules

Flutamide, an acetanilid, nonsteroidal, orally active antiandrogen, has the chemical name, 2-methyl-*N*-[4-nitro-3-(trifluoromethyl)phenyl]propanamide. Each capsule contains 125 mg of flutamide. The inactive ingredients include: cornstarch, lactose, magnesium stearate, povidone, and sodium lauryl sulfate. Gelatin capsule shells may also contain benzyl alcohol, butylparaben, colloidal silicon dioxide, edetate calcium disodium, methylparaben, propylparaben, and sodium propionate, as well as the following dye systems: FD&C Blue No. 1, FD&C Red No. 3, FD&C Yellow No. 6, titanium dioxide, and black ink.

Fluticasone Propionate and Salmeterol Xinafolate Inhalation Powder

This is a combination of fluticasone propionate and salmeterol xinafolate. One active component, fluticasone propionate, is a corticosteroid that has the chemical name S-(fluoromethyl)6(α),9-difluoro-11(β), 17-dihydroxy-16(α)-methyl-3-oxoandrosta-1, 4-diene-17(β)-carbothioate, 17-propionate. The other active component is salmeterol xinafolate, a highly selective beta 2-adrenergic bronchodilator. Salmeterol xinafolate is the racemic form of the 1-hydroxy-2-naphthoic acid salt of salmeterol. The chemical name of salmeterol xinafolate is 4-hydroxy-(α)1-[[[6-(4-phenylbutoxy)-hexyl]amino] methyl]-1,3-benzenedimethanol,1-hydroxy-2-naphthalenecarboxylate. These are specially designed plastic devices containing a double-foil blister strip of a powder formulation of fluticasone propionate and salmeterol xinafolate intended for oral inhalation only. Each blister on the double-foil strip within the device contains 100, 250, or 500 mcg of microfine fluticasone propionate and 72.5 mcg of microfine salmeterol xinafolate salt, equivalent to 50 mcg of salmeterol base, in 12.5 mg of formulation containing lactose. Each blister contains one complete dose of both medications. After a blister containing the medication is opened by activating the device, the medication is dispersed into the airstream created by the patient inhaling through the mouthpiece. Under standardized *in vitro* test conditions, it delivers 93, 233, and 465 mcg of fluticasone propionate and 45 mcg of salmeterol base per blister, respectively, when tested at a flow rate of 60 l/min for 2 sec.

Fluvastatin Sodium Capsules

Fluvastatin sodium is a water-soluble cholesterol-lowering agent, which acts through the inhibition of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. It is supplied in capsules containing fluvastatin sodium, equivalent to 20 mg or 40 mg of fluvastatin, for oral administration. The inactive ingredients in the capsules are: gelatin, magnesium stearate, microcrystalline cellulose, pregelatinized starch (corn), red iron oxide, sodium lauryl sulfate, talc, titanium dioxide, and yellow iron oxide. Capsules may also include: benzyl alcohol, black iron oxide, butylparaben, carboxymethylcellulose sodium, edetate calcium disodium, methylparaben, propylparaben, silicon dioxide, and sodium propionate.

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
20.00	1	Fluvastatin	20.00
62.84	2	Calcium Carbonate Heavy Precipitated	62.84
2.00	3	Sodium Bicarbonate	2.00
23.35	4	Microcrystalline Cellulose Avicel PH102	23.35
20.95	5	Pregelatinized Starch (Starch 1500)	20.95
QS	6	Water Purified	QS
33.88	7	Microcrystalline Cellulose	33.38
20.95	8	Pregelatinized Starch	20.95
9.43	9	Talc	9.43
1.05	10	Magnesium Stearate	1.05

MANUFACTURING DIRECTIONS

1. The fluvastatin (Item 1), sodium bicarbonate (Item 3), calcium carbonate (Item 2), microcrystalline cellulose (Item 4), and pregelatinized starch (Item 5) are mixed for 5 min, and the mixture is passed through a 40-mesh screen and blended for another 3 min.
2. Water is added to the mixture, while blending for about 4 min to form a wet granulation.
3. The wet granulation is dried in a fluid bed dryer at 50°C inlet temperature to a loss on drying of 1.59%.
4. The dried granules are passed through a 20-mesh screen and blended with the microcrystalline cellulose and pregelatinized starch set-asides (Items 7 and 8) for about 10 min.
5. Talc and magnesium stearate (each prescreened on a 60-mesh bolting cloth) are added to the mixture while blending for about 5 min. The resulting composition has a loss on drying of 2.65%.
6. A blue opaque capsule is filled with the composition and polished manually with salt.

Formoterol Fumarate Inhalation Powder

This consists of a capsule dosage form containing a dry powder formulation of formoterol fumarate intended for oral inhalation only with the AerolizerJ® inhaler. Each clear, hard gelatin capsule contains a dry powder blend of 12 mcg of formoterol fumarate and 25 mg of lactose as a carrier. The active component is formoterol fumarate — a racemate.

Formoterol Fumarate Inhaler Capsules

The inhaler consists of a capsule dosage form containing a dry powder formulation of formoterol fumarate intended for oral inhalation only with the AerolizerJ inhaler. Each clear, hard gelatin capsule contains a dry powder blend of 12 mcg of formoterol fumarate and 25 mg of lactose as a carrier.

Fosfomycin Tromethamine Sachets

Fosfomycin tromethamine sachet contains fosfomycin tromethamine, a synthetic, broad-spectrum, bactericidal antibiotic for oral administration. It is available as a single-dose sachet, which contains white granules consisting of 5.631 g of fosfomycin tromethamine (equivalent to 3 g of fosfomycin) and the following inactive ingredients: mandarin flavor, orange flavor, saccharin, and sucrose.

Gabapentin Capsules

Gabapentin capsules are supplied as imprinted hard shell capsules containing 100 mg, 300 mg, and 400 mg of gabapentin, The inactive ingredients for the capsules are: lactose, cornstarch, and talc. The 100 mg capsule shell contains gelatin and titanium dioxide. The 300 mg capsule shell contains gelatin, titanium dioxide, and yellow iron oxide. The 400-mg capsule shell contains gelatin, red iron oxide, titanium dioxide, and yellow iron oxide. The imprinting ink contains FD&C Blue No. 2 and titanium dioxide.

Ganciclovir Capsules

Ganciclovir is a synthetic guanine derivative that is active against cytomegalovirus. It is available as 250 mg and 500 mg capsules. Each capsule contains 250 mg or 500 mg ganciclovir, respectively, and the following inactive ingredients: croscarmellose sodium, magnesium stearate, and povidone. Both hard gelatin shells consist of gelatin, titanium dioxide, yellow iron oxide, and FD&C Blue No. 2.

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
250.00	1	Ganciclovir	250.00
3.00	2	Magnesium Stearate	3.00
30.00	3	Cornstarch	30.00
116.00	4	Lactose	116.00
4.00	5	Polyvinylpyrrolidone	3.00
QS	6	Methanol	QS

MANUFACTURING DIRECTIONS

1. Items 1, 3, and 4 are granulated in a solution of Item 5 in Item 6.
2. Granules are dried, lubricated with Item 2, and filled in capsules or tableted.

Gemfibrozil Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
100.00	1	Gemfibrozil	100.00
248.80	2	Lactose Anhydrous[a]	248.80
100.00	3	Cornstarch	100.00
25.00	4	Sodium Starch Glycolate	25.00
5.00	5	Povidone	5.00
15.00	6	Polysorbate 80	15.00
1.25	7	Colloidal Silicon Dioxide	1.25
5.00	8	Magnesium Stearate	5.00
QS	9	Water Purified	QS

[a] The quantity of lactose can be reduced to compensate if additional quantities of glycine 12.5 mg and citric acid 2.5 mg are used.

MANUFACTURING DIRECTIONS

1. An aqueous wet granulation process is used whereby the respective active ingredients of lactose, cornstarch, sodium starch glycolate, colloidal silicon dioxide, and povidone are mixed and subsequently granulated with polysorbate dissolved in purified water.
2. Additional purified water is then added until granules form and no dry powder remains.
3. Wet granules are dried at 60°C until the loss on drying is not more than 2%.
4. The dried granules are milled with the sodium starch glycolate, blended, and lubricated with screened magnesium stearate in a twinshell blender.
5. Size 0 capsules are used to fill 500 mg of granules.

Glycoprotein IIa/IIb Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
0.23	1	Glycoprotein IIa/IIb	0.23
53.77	2	Lactose Anhydrous	53.77
2.70	3	Crospovidone	2.70
1.20	4	Povidone	1.20
1.50	5	Disodium Citrate	1.50
0.60	6	Magnesium Stearate	0.60
QS	7	Water Purified	QS

MANUFACTURING DIRECTIONS

1. Triturate Item 1 with Item 2 (portion) in a small mixing vessel or mortar.
2. Charge the balance of Item 2 and two-thirds of the quantity of Item 3 in a shear granulator, and add Step 1 into it with fast mixing.
3. Granulate Step 2 using aqueous solution of balance of Item 4 and Item 5 (9.3% solids in Item 7 and pH adjusted to 4 using 1 N hydrochloric acid).
4. Screen the granulation through a No. 8 mesh and dry in vacuum at 40°C to a moisture content of 0.7%.
5. Blend the granulation with remaining amount of Items 3 and 6.
6. Fill 60 mg in size 3 capsules.

Guaifenesin Sustained-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
150.00	1	Guaifenesin	150.00
26.60	2	Carbopol 934P (B.F. Goodrich)	26.60
172.10	3	PVP C-15 (GAF Corporation)	172.10
3.50	4	Talc	3.50
1.80	5	Zinc Stearate	1.80

MANUFACTURING DIRECTIONS

1. The Carbopol 934P, PVP C-15, talc, and zinc stearate are combined in a mortar and triturated well.
2. The guaifenesin is added to this mixture in the mortar and triturated well until a substantially uniform particulate mixture is achieved.
3. The resulting particulate mixture is filled 354 mg into size 1 hard gelatin capsule shells.

Herbal AIDS Treatment Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
32.00	1	*Combretum quadrangulare*	32.00
20.00	2	*Houttuynia cordata*	20.00
20.00	3	*Mimusops elengi*	20.00
20.00	4	*Randia siemensis*	20.00
308.00	5	*Borassus flabellifer*	308.00

MANUFACTURING DIRECTIONS

1. Items 1–5 are prepared by first making a powdered form of herbs, extracting them in water or hydroalcoholic solution, and drying the extract.
2. Powdered extracts 1–5 are admixed and filled in a gelatin capsule. Add magnesium stearate 1%, if necessary, to improve flow.

Histadine Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
250.00	1	Histadine	240.00
QS	2	Lactose	QS

MANUFACTURING DIRECTIONS

1. Mix Items 1 and 2 (using desired quantity of Item 2 to fit the capsule size chosen) by process of trituration.
2. Fill in appropriate capsule.

Human Growth Hormone Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
28.00 IU	1	Human Growth Hormone[a]	28,000 IU
0.047	2	Dimyristoyl Phosphatidic Acid	0.047
3.38	3	Aprotinin[b]	3.38
3.47	4	Sodium Cholate	3.47
3.70	5	Polyoxy-23 Lauryl Ether	3.70
138.60	6	Polyethylene Glycol 400	138.60
13.71	7	Propylene Glycol	13.71
8.67	8	Water/pH Adjuster	8.67
30.92	9	Cholesterol	30.92
17.40	10	Tween 80	17.40
62.53	11	Egg Yolk Lecithin	62.53
19.43	12	d-alpha Tocopherol	19.43
27.64	13	Sorbitan Monooleate	27.64
246.90	14	Isostearic Acid	246.90

[a] Human growth hormone 2.6 IU = 1 mg.
[b] Aprotinin: 7,500 KIU = 1 mg.

MANUFACTURING DIRECTIONS

1. Polyoxy-23 lauryl ether (commercially available as Brij™ 35) is dispersed in the solvent mixture of polyethylene glycol 400 and propylene glycol.
2. Sodium cholate is also separately dispersed in the mixture.
3. A water solution containing recombinant human growth hormone, phospholipid, and aprotinin is then added to the solvent mixture in Step 1 and the pH is adjusted to 7.5–7.8 with the help of a phosphate buffer.
4. The lipid solution is made separately in another beaker.
5. To the oil solution, the polyol solution is added dropwise while mixing continuously. While mixing, it is suggested that the vessel be ice jacketed to prevent the denaturation of the protein in the formulation.
6. A clear transparent liquid, which is called the preemulsion solution, is obtained after approximately 5 min of mixing at low speed. An *in situ* emulsion can be made by mixing any ratio of the preemulsion solution with the simulated intestinal fluid.
7. The preemulsion solution is filled in a size 0 hard gelatin capsule and the capsule is sealed with a band of gelatin solution. The banding helps to coat the capsule uniformly.
8. The capsule is then coated with a 10% hydroxypropyl methylcellulose solution as an undercoat. The amount of coat required is sufficient just enough to cover the capsule uniformly with a thin layer of the polymer coat. Usually, 3.5–4.5% weight gain of the capsule is a good indication of the amount required as an undercoat.
9. Once the capsule is coated with an undercoat, enteric coating is applied. For enteric coating purposes, different polymers, such as hydroxypropyl methylcellulose, hydroxypropyl methylcellulose phthalate, and cellulose acetate phthalate are used.
10. Anionic copolymers which are based on methacrylic acid and methyl methacrylate, commercially available as Eudragit, are also very suitable polymers for enteric coating purposes. The polymer is dissolved in organic solvents such as ethyl alcohol, methyl alcohol, acetone, and isopropyl alcohol. A combination of two solvents can also be used. The amount of enteric coating solution required is 5–6% weight gain of the capsules from the original weight of the capsules before applying enteric coat. A typical enteric coating solution is made as follows:

Methacrylic acid and methyl methacrylate copolymer 10% w/w
Diethyl butyl phthalate (plasticizer) 2% w/w
Acetone 22% w/w
Isopropanol 66% w/w

Procedure:

Mix acetone and isopropanol. Add the polymer slowly with constant mixing. Once the polymer is dissolved, add the plasticizer slowly and let it dissolve.

For a size 0 capsule, the previously mentioned enteric coating solution can be sprayed using fluidizing bed techniques. The fluid-bed sprayer/dryer is operated with the following parameters:

Flow rate: 1.5 ml/min
Inlet air temperature: 25°C
Outlet air temperature: 25°C
Air flap: 35
Atomizer: 2.0 bar

A size 0 capsule, after the enteric coating, will typically have the following composition:

Preemulsion solution: 0.589 g
Undercoat polymer: 0.027 g
Enteric coat polymer: 0.032 g, 0.648 g

Hydrochlorothiazide and Triamterene Capsules

This is a combination capsule with an opaque red cap and an opaque white body. It contains hydrochlorothiazide (25 mg) and triamterene (37.5 mg). Hydrochlorothiazide is a diuretic/antihypertensive agent, and triamterene is an antikaliuretic agent. Triamterene is 2,4,7-triamino-6-phenylpteridine. Inactive ingredients consist of benzyl alcohol, cetylpyridinium chloride, D&C Red No. 33, FD&C Yellow No. 6, gelatin, glycine, lactose, magnesium stearate, microcrystalline cellulose, povidone, polysorbate 80, sodium starch glycolate, titanium dioxide, and trace amounts of other inactive ingredients. These capsules meet Drug Release Test 3 as published in the USP monograph for Triamterene and Hydrochlorothiazide Capsules.

Hydrochlorothiazide Capsules

Hydrochlorothiazide is the 3,4-dihydro derivative of chlorothiazide. Its chemical name is 6-chloro-3,4-dihydro-2 *H*-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide. It is supplied as 12.5 mg capsules for oral use. Each capsule contains the following inactive ingredients: colloidal silicon dioxide, cornstarch, D&C Red No. 28, D&C Yellow No. 10, FD&C Blue No. 1, gelatin, lactose monohydrate, magnesium stearate, titanium dioxide, and other optional ingredients.

Hydroxyzine Pamoate Capsules and Oral Suspension

Hydroxyzine pamoate is designated chemically as 1-(p-chlorobenzhydryl) 4-[2-(2-hydroxyethoxy) ethyl] diethylenediamine salt of 1,1'-methylene bis (2-hydroxy-3-naphthalene carboxylic acid). The inert ingredients for the capsule formulations are: hard gelatin capsules (which may contain FD&C Yellow No. 10, FD&C Green No. 3, FD&C Yellow No. 6, FD&C Red No. 33, and other inert ingredients); magnesium stearate; sodium lauryl sulfate; starch; and sucrose. The inert ingredients for the oral suspension formulation are: carboxymethylcellulose sodium; lemon flavor; propylene glycol; sorbic acid; sorbitol solution; and water.

Hyoscyamine Sulfate Capsules

Hyoscyamine sulfate is one of the principal anticholinergic/antispasmodic components of belladonna alkaloids. Chemically, it is benzeneacetic acid, (alpha)-(hydroxymethyl)-,8-methyl-8-azabicyclo[3.2.1.]oct-3-ylester,[3(S)-endo]-,sulfate (2:1), dihydrate. The sustained release capsules contain 0.375 mg hyoscyamine sulfate in an extended-release formulation designed for oral b.i.d. dosage. Each capsule also contains the following inactive ingredients: FD&C Blue No. 1, D&C Red No. 28, FD&C Red No. 40, FD&C Yellow No. 6, gelatin, lactose monohydrate, sodium lauryl sulfate, magnesium stearate, silicon dioxide, titanium dioxide, and other optional ingredients.

Ibuprofen Microencapsulated Sustained-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
450.00	1	Ibuprofen	450.00
450.00	2	Sodium Alginate	450.00
4.50 ml	3	Zinc Chloride Solution 2%	451.00
QS	4	Hydrochloric Acid	QS
0.22 ml	5	Glycerin	225.00 ml
—	6	Water Purified	22.5 l

MANUFACTURING DIRECTIONS

1. A mixture consisting of Item 1, previously triturated in 225 ml of glycerin, is added with rapid stirring to an aqueous solution consisting of 450 g (w/v) of sodium alginate in 22.5 l of purified water.
2. This solution is then added to 45 l of a 2% (w/v) zinc chloride solution, which has previously been adjusted to pH 3 by the addition of HCl while the rapid stirring is continued for 10 min.
3. The preparation is then allowed to stand at room temperature for 4 h, after which the drug-entrapped zinc alginate precipitate is collected by filtration, washed three times with distilled water, and dried under vacuum for 24 h.
4. After drying, the residue is granulated using minimal amounts of glycerin/water and processed into 0.5-mm diameter microspheres by mechanical extrusion and spheronization (Nica Extruder®; Aeromatic Ltd., Bubendorf, Switzerland), into which the slightly flexible mass represented by the above residue is fed, and which produces therefrom a continuous flow of cylindrical extrudate that is 0.5 mm in diameter.
5. This extrudate falls onto the spinning plate of a Nica Spheronizer® (Aeromatic Ltd.), where it is broken into cylinders of approximately 1:1 length:diameter ratio. Interaction then between the spinning disc and the wall of the spheronizer causes the cylinders to be worked into spheres of 0.5 mm diameter.
6. The spheres are then filled into gelatin capsules (1 g of spheres per size 0 capsule, which represents a total dose of 450 mg of ibuprofen). The capsules of spheres thus produced represent a sustained-release dosage form for analgesic–antipyretic activity with less propensity for gastrointestinal side effects than the conventional tablet form of ibuprofen. Upon ingestion, the spheres begin to release the incorporate drug almost immediately, but begin erosion in 3 to 5 h. Total erosion time is approximately 8 h.

Ibuprofen Sustained-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
800.00	1	Ibuprofen	800.00
8.00	2	Aerosil R972	8.00
8.00	3	Beeswax	8.00

MANUFACTURING DIRECTIONS

1. Charge Items 1 and 3 in a jacketed kettle, and heat to melt; stir until uniformly melted.
2. Add Item 2, with stirring, to form a homogeneous suspension. Allow to cool.
3. Pass through sieve. If needed, a lubricant may be added to facilitate flow (1% magensium stearate).
4. Fill size 00 capsules.
5. The 50% dissolution time is approximately 15 h.

Given below are guidelines on controlling release rates of ibuprofen using different compositions of excipients. In all instances, ibuprofen is melted with the ingredient, allowed to congeal, sized, and filled in appropriate size capsules. T_{50} represents time for 50% dissolution. A combination of these granules can be used to provide a wide range of ibuprofen release patterns that are particularly useful in arthritis therapy.

	Amount of		
	Ibuprofen (% w/w)	**Excipient (% w/w)**	**T_{50} (hours)**
None	100	—	2.9
Arachis oil	90	10	4.1
Beeswax	90	10	>24.0
Beeswax	90[a]	10	9.5
Colloidal silicon dioxide (Aerosil 200)	99	1	4.7
	97	3	6.6
	95	5	10.0
Colloidal silicon dioxide (Aerosil R972)	99	1	5.9
	95	5	20.5
Croscarmellose sodium (AcDiSol®)	99	1	0.4
	97.5	2.5	0.13
Glycerides	95	5	3.0
(Gelucire 50/13)	90	10	7.4
(Gelucire 50/13)	90[a]	10	2.9
Liquid paraffin	90	10	4.8
Cornstarch	99	1	3.5
	95	5	1.6
	90	10	0.16
Copolymer (Pluronic F68)	95	5	3.0
PEG 400	90	10	3.5
PEG 4000	90	10	3.3
PEG 6000	90	10	4.2
Polyvinylpyrrolidone (Crospovidone)	90	10	4.0
Sodium starch glycolate (Explotab®)	99	1	1.8
	95	5	0.3
Stearic acid	99	1	4.2
	95	5	7.8
	90	10	>24.0
Stearyl alcohol	99	1	10.0
	95	5	14.0
	90	10	>24.0

[a] Indicates S(+)ibuprofen.

Ifosfamide Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
250.00	1	Ifosfamide	250.00
83.50	2	Microcrystalline Cellulose, Avicel PH105	83.50
1.50	3	Colloidal Silicon Dioxide	1.50
0.50	4	Magnesium Stearate	0.50

MANUFACTURING DIRECTIONS

1. Pass Items 1–3 through a 0.8-mm sieve into a blender.
2. Blend for 4 min.
3. Add Item 4, which has been sieved through a 0.8-mm sieve, to Step 2; mix for another 1 min.
4. Fill in size 1 capsule, 340 mg each. For a 500-mg capsule, fill 680 mg in size 00 capsules.
5. To impart enteric resistance to capsules, coat using a coating suspension. For example, to coat 2500 size 1 capsules containing 250 mg ifosfamide, use 3 kg of suspension containing 1440 g anionic polymerizate of methacrylic acid and methacrylic acid esters with a mean molecular weight of, for example, 150,000, to which a conventional softener has been added, 18 g of 1,2-propandiol, 36 g of magnesium stearate, and 1506 g of isopropanol. The copolymerizate of methacrylic acid and methylmethacrylate that may, for example, be considered is Eudragit® L, particularly in the form of a 12.5% solution in isopropanol (Eudragit® L RTM /12.5%). Copolymerizates for this type are soluble in neutral to weakly alkaline medium through salt formation with alkalis.

Imatinib Mesylate Capsules

The capsules contain imatinib mesylate equivalent to 100 mg of imatinib freebase. Imatinib mesylate is designated chemically as 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-henyl]benzamide methanesulfonate. The inactive ingredients are: colloidal silicon dioxide, crospovidone, magnesium stearate, and microcrystalline cellulose. The capsule shell contains gelatin; iron oxide; red (E172); iron oxide, yellow (E172); and titanium dioxide (E171).

Indinavir Sulfate Capsules

Indinavir sulfate is an inhibitor of the human immunodeficiency virus (HIV) protease. The chemical name for indinavir sulfate is [1(1*S,2R),*5(*S)*]-2,3,5-trideoxy-*N*-(2,3-dihydro-2-hydroxy-1*H*-inden-1-yl)-5-[2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinyl-methyl)-1-piperazinyl]-2-(phenylmethyl)-D-*erythro*-pentonamide sulfate (1:1) salt. Capsules are formulated as a sulfate salt and are available for oral administration in strengths of 100, 200, 333, and 400 mg of indinavir (corresponding to 125, 250, 416.3, and 500 mg indinavir sulfate, respectively). Each capsule also contains the inactive ingredients anhydrous lactose and magnesium stearate. The capsule shell has the following inactive ingredients and dyes: gelatin, titanium dioxide, silicon dioxide, and sodium lauryl sulfate.

Scale (mg/Caps)	Item	Material Name	Qty/1000 Caps (g)
400.00	1	Indinavir Sulfate, USE Invinavir Sulphate	400.00
7.00	2	Sodium Lauryl Sulphate	7.00
1.50	3	Colloidal Silicon Dioxide (Aerosil-200)	1.50
6.50	4	Magnesium Stearate	6.50
650.00	5	Lactose Monohydrate Dense QS to	650.00
1	6	Empty Hard Gelatin Capsule, size 00	1000

MANUFACTURING DIRECTIONS

1. Sift indinavir sulphate, lactose anhydrous, and Aerosil-200 through a specified sieve.
2. Load the sifted powder into a blender, and blend well.
3. Sift magnesium stearate and sodium lauryl sulphate through a specified sifter.
4. Mix Step 3 with Step 2, and blend well.
5. Encapsulate the powder to get the stated amount of indinavir per capsule.

Indomethacin Capsules

Indomethacin cannot be considered a simple analgesic and should not be used in conditions other than those recommended. Capsules for oral administration contain either 25 mg or 50 mg of indomethacin and the following inactive ingredients: colloidal silicon dioxide, FD&C Blue No. 1, FD&C Red No. 3, gelatin, lactose, lecithin, magnesium stearate, and titanium dioxide. Suspension for oral use contains 25 mg of indomethacin per 5 ml, alcohol 1%, and sorbic acid 0.1% added as a preservative. The suspension also contains the following inactive ingredients: antifoam AF emulsion, flavors, purified water, sodium hydroxide or hydrochloric acid to adjust pH, sorbitol solution, and tragacanth.

1.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
25.00	1	Indomethacin Micronized	26.25
1.00	2	Lecithin (Liquid)	1.00
—	3	Trichloro Trifluoro Ethane	17.00
218.25	4	Lactose Monohydrate (Dense)	218.25
1.50	5	Colloidal Silicon Dioxide (Aerosil 200)	1.50
2.00	6	Sodium Lauryl Sulfate	2.00
1.00	7	Magnesium Stearate	1.00
1	8	Empty Hard Gelatin Capsule, Size 3	1000

MANUFACTURING DIRECTIONS

I. Precautions
   A. The processing area must be under controlled room temperature and humidity. The limits are: RH: 40–50%; temperature: 21–27°C.
   B. Trichloro trifluoro ethane is a volatile substance when kept in open air. Always keep in covered containers.
   C. Do not expose the granules for a long time to light as discoloration will occur.
   D. Mix Item 2 with Item 3 in a clean stainless steel container. Firmly cover to avoid any vaporization.

II. Blending
   A. Mix Item 1 and 0.25 g of Item 5 in a drum mixer.
   B. Sift the "mix" through 1250-µm sieve using sifter. Collect in stainless steel drum and transfer to the mixer.
   C. Add Item 2 solution from Step 1 to the Item 1 powder in mixer while mixing at high speed. When the addition is over, mix the moist mass at highest speed for 5 min.
   D. Scrape the sides of mixer and mix at highest speed for 5 min.
   E. Again, scrape the sides of mixer and mix at highest speed for 10 min.

III. Drying
   A. Spread the moist mass thinly on stainless steel trays. Break the big lumps if any.
   B. Dry the mass in oven using only cold air (without temperature) for 6 h.

IV. Sifting
   A. Sift 168.25 g of Item 4 through 630-µm sieve, using a sifter. Collect in stainless steel drum. Keep aside.

V. Mixing
   A. Mix 50.0 g of Item 4, the indomethacin–lecithin mixture (dried), and 1.25 g of Item 5 in a drum mixer, for 10 min.
   B. Sift the mixture twice through 630-µm stainless steel sieve, using a sifter.
   C. Use Item 4 (about 2–4 g) to prevent the clogging of the sifter sieve, if required.
   D. Load sieved Item 4 from Step 4 into the blender.
   E. Add lactose–indomethacin–aerosil mixture from Step V-B to the blender. Mix for 10 min.

VI. Lubrication
   A. Sift Items 6 and 7 through a 630-µm sieve, using a sifter.
   B. Add to the powder in blender. Mix for 2 min.
   C. Unload the granules in stainless steel drums.

VII. Loading of Empty Shells
   A. Load the empty capsule shells (size 3) in the hopper.
   B. Run the machine and check the locking of shells.

VIII. Filling of Powder
   A. Calculation: A fill weight of one capsule = 250 mg.

2.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
25.00	1	Indomethacin	25.00
0.50	2	Lecithin Swiss	0.50
1.25	3	Colloidal Silicon Dioxide	1.25
1.67	4	Magnesium Stearate	1.67
200.00	5	Lactose	200.00
—	6	Chloroform	QS

3.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
50.00	1	Indomethacin	50.00
1.00	2	Lecithin Swiss	1.00
3.00	3	Colloidal Silicon Dioxide	3.00
4.00	4	Magnesium Stearate	4.00
325.00	5	Lactose	325.00
—	6	Chloroform	QS

MANUFACTURING DIRECTIONS

1. Mix indomethacin with about one-half of the quantity of lactose, and micronize.
2. Dissolve lecithin in chloroform, and wet this solution with the remaining half of the lactose.
3. Dry the chloroform mixture in a drying oven at 4°C for 4 h.
4. Pass the dried granulate through a Fitz mill sieve No. 24228 at a low speed; add the mixture of indomethacin and lactose from Step 1; add colloidal silicon dioxide and magnesium stearate, and mix for 15 min.
5. Fill into size 3 capsules as 200 mg ± 5%. For 50 mg capsules, fill into capsules as 325 mg ± 5%.

Indomethacin Microencapsulated Sustained-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
45.00	1	Indomethacin	45.00
45.00	2	Sodium Alginate	45.00
4.50 ml	3	Zinc Chloride Solution 2%	45 l
QS	4	Hydrochloric Acid	QS
0.22	5	Glycerin	22.5 ml
—	6	Water Purified	2.25

MANUFACTURING DIRECTIONS

1. A mixture consisting of Item 1 previously triturated in 22.5 ml glycerin is added with rapid stirring to an aqueous solution consisting of 45.00 g (w/v) of sodium alginate in 2.25 l of purified water.
2. This solution is then added to 4.5 l of a 2% (w/v) zinc chloride solution, which has previously been adjusted to pH 3 by the addition of HCl, while the rapid stirring is continued for 10 min.
3. The preparation is then allowed to stand at room temperature for 4 h, after which the drug-entrapped zinc alginate precipitate is collected by filtration, washed three times with distilled water, and dried under vacuum for 24 h.
4. After drying, the residue is granulated using minimal amounts of glycerin/water and processed into 0.5-mm diameter microspheres by mechanical extrusion and spheronization (Nica Extruder®; Aeromatic Ltd., Bubendorf, Switzerland), into which the slightly flexible mass represented by the above residue is fed, and which produces therefrom a continuous flow of cylindrical extrudate that is 0.5 mm in diameter.
5. This extrudate falls onto the spinning plate of a Nica Spheronizer® (Aeromatic Ltd.), where it is broken into cylinders of approximately 1:1 length:diameter ratio. Interaction between the spinning disc and the wall of the spheronizer then causes the cylinders to be worked into spheres of 0.5 mm in diameter.
6. The spheres are then filled into gelatin capsules (100 mg of spheres per size 1 capsule, which represents a total dose of 45.0 mg indomethacin). The capsules of the spheres thus produced represent a sustained-release dosage form for analgesic–antipyretic activity with less propensity for gastrointestinal side effects than the conventional tablet form of indomethacin. Upon ingestion the spheres begin to release the incorporate drug almost immediately, but begin to erode in 3–5 h. Total erosion time is approximately 8 h.

Indomethacin Sustained-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
75.00	1	Indomethacin	75.00
110.20	2	Sucrose	110.20
39.75	3	Cornstarch	39.75
36.20	4	Lactose	36.20
10.95	5	Polyvinylpyrrolidone	10.95
19.65	6	Talc	19.65
5.15	7	Magnesium Stearate	5.15
1.10	8	Eudragit L	1.10
2.00	9	Eudragit S	2.00
—	10	Ethyl Alcohol	98.55
—	11	Acetone	27.90

MANUFACTURING DIRECTIONS

I. Pellets
   A. Weigh and mix in a stainless steel mixer suitable quantities of sucrose and cornstarch in the proportion of 3:1 w/w. Sift through a screen of suitable size to break up possible lumps.
   B. Transfer the mixture to a stainless steel coating pan and adjust rotary speed between 20 and 30 rpm so as to obtain good tumbling action.
   C. By means of a suitable spray gun, spray over the powder a quantity of water equal to 15% w/w in very minute drops.
   D. Place the wet pellets over a thermostatic tray dryer and dry at 37°C to complete evaporation of water.
   E. Pass the dried pellets through sieves of suitable screens to ensure removal of dust and selection of cores of desirable size.

II. Active Pellets
   A. Dissolve polyvinylpyrrolidone in ethyl alcohol and add indomethacin previously mixed with lactose (No. 3) to it.
   B. Transfer 149.95 kg of neutral pellets obtained from Step I-E to a stainless steel coating pan and adjust the rotary speed between 20 and 30 rpm so as to obtain good tumbling action.
   C. Spray over the neutral pellets the result of Step II-A.
   D. Keep the pan rotating to allow partial evaporation of the solvent.
   E. Complete evaporation of the solvent by drying the pellets in a thermostat at 35°C for 3 days.

III. Film-Coated Pellets
   A. Dissolve Eudragit L and Eudragit S in acetone.
   B. Transfer the active pellets obtained from Step II-E to a stainless steel coating pan, and adjust the rotary speed to obtain a good tumbling action.
   C. Spray the pellets as uniformly as possible with the solution obtained from Step II-E.
   D. Spray the wet pellets with talc and magnesium stearate to prevent agglutination.
   E. Keep the pan rotating to achieve solidification of the film coating and partial evaporation of the solvent.
   F. Complete evaporation of the solvent by drying the pellets in a thermostat for 35°C for 3 days.

IV. Blending of Pellets
   A. Transfer the film-coated pellets obtained from Step III-F to a stainless steel pan and add a suitable quantity of neutral pellets obtained from Step I-E so as to obtain the required dosage.
   B. Add a 0.5% w/w of talc to eliminate electrostatic charges and mix for 30–35 min.

V. Filling
   A. Fill the blended pellets obtained from Step IV-B into capsules (size 2) at the dose of 300 mg each.

Insulin Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
140.00 IU	1	Insulin[a]	140,000 IU
0.047	2	Dimyristyl Phosphatidyl Choline	0.047
3.39	3	Aprotinin[b]	3.39
3.76	4	Hydroxypropyl Cellulose-LF	3.76
3.76	5	Polyoxy-40 Stearate Myrj-52®	3.76
139.80	6	Polyethylene Glycol 400	139.80
15.57	7	Propylene Glycol	15.57
8.75	8	Water-Citrate Buffer for pH adjustment	8.75
31.20	9	Cholesterol	31.20
17.56	10	Tween 80	17.56
63.10	11	Egg Yolk Lecithin	63.10
27.90	12	Glyceryl Amino Oleate	27.90
19.60	13	d-alpha Tocopherol	19.60
249.10	14	Oleic Acid	249.10

[a] Insulin: 26 IU = 1 mg
[b] Aprotinin: 7500 KIU = mg

Manufacturing Directions

1. Insulin is a biologically active proteinaceous material. Insulin is a polypeptide consisting of 65 amino acids with an approximate molecular weight of 6000. In its preparations, there can be no use of heat or alcohol that can denature it.
2. The overall method is as follows: The surfactant Myrj-52 is slowly dispersed into the mixture of polyethylene glycol 400 and propylene glycol. Once it dissolves, hydroxypropyl cellulose as a stabilizer is also added, which is dispersed slowly into the preceding mixture. A separate solution of the proteinaceous material along with the phospholipid and the protease inhibitor is made in a portion of the preceding solvent mixture. The solution can then be added to the PEG/PG mixture at room temperature. The amount of any water is limited to 5% of the polyol solvent. When the water solution is used, citrate buffer is used to maintain the pH at a point where the protein is most stable. In this particular example, if insulin is used, it is suggested that the pH be maintained with a citrate buffer at or around 2.5. Separately, the ingredients of the lipid solvent are mixed together. Under gentle and constant stirring, the polyol solution is dispersed with the lipid solution.
3. The surfactant (Polyoxy-40 stearate) is slowly dispersed into a mixture of polyethylene glycol and propylene glycol.
4. Once it is dissolved, small amounts of hydroxypropyl cellulose are then added and dispersed into the same mixture.
5. Insulin is dissolved in water, and citric acid is dissolved in water for maintaining the pH at 2.5.
6. The water solution is added to the polyethylene glycol mixture. In a separate vessel, dissolve all the ingredients of the oil phase in oleic acid.
7. Cholesterol is added slowly to achieve faster dissolution.
8. Once both the phases are ready, the polyol solution is added slowly to lipid phase while mixing at low speed. The vessel should be preferably ice jacketed because heat may be produced. Once the addition is achieved, a transparent yellowish-brown solution is obtained.
9. The preemulsion solution is filled in a size 0 hard gelatin capsule, and the capsule is sealed with a band of gelatin solution. The banding helps to coat the capsule uniformly.
10. The capsule is then coated with a 10% hydroxypropyl methylcellulose solution as an undercoat. The amount of coat required is sufficient just enough to cover the capsule uniformly with a thin layer of the polymer coat. Usually, 3.5–4.5% weight gain of the capsule is a good indication of the amount required as an undercoat.

11. Once the capsule is coated with an undercoat, enteric coating is applied. For enteric coating purposes, different polymers, such as hydroxypropyl methylcellulose, hydroxypropyl methylcellulose phthalate, and cellulose acetate phthalate are used.
12. Anionic copolymers that are based on methacrylic acid and methyl methycralate, commercially available as Eudragit, are also very suitable polymers for enteric coating purposes. The polymer is dissolved in organic solvents such as ethyl alcohol, methyl alcohol, acetone, and isopropyl alcohol. A combination of two solvents can also be used. The amount of enteric coating solution required is 5–6% weight gain of the capsules from the original weight of the capsules before applying enteric coat. A typical enteric coating solution is made as follows:

    Methacrylic acid and methyl methycralate copolymer 10% w/w
    Diethyl butyl phthalate (plasticizer) 2% w/w
    Acetone 22% w/w
    Isopropanol 66% w/w

    Procedure:
    Mix acetone and isopropanol. Add the polymer slowly with constant mixing. Once the polymer is dissolved, add the plasticizer slowly, and let it dissolve.
    For a size 0 capsule, the previously mentioned enteric coating solution can be sprayed using fluidizing-bed techniques. The fluid-bed sprayer/dryer is operated with the following parameters:
        Flow rate: 1.5 ml/min
        Inlet air temp.: 25°C
        Outlet air temp.: 25°C
        Air flap: 35

    Atomizer: 2.0 bar
    A size 0 capsule after the enteric coating will typically have the following composition:
        Preemulsion solution: 0.589 g
        Undercoat polymer: 0.027 g
        Enteric coat polymer: 0.032 g, 0.648 g

Iron-Polysaccharide Complex Capsules

Each bead-filled capsule contains 150 mg elemental iron as polysaccharide — iron complex, as cell-contracted akaganéite. Each capsule also contains the following inactive ingredients: D&C Red No. 7, D&C Red No. 28, D&C Yellow No. 10, FD&C Blue No. 1, FD&C Red No. 40, FD&C Yellow No. 6, gelatin, hydrogenated castor oil, polysorbate 80 pharmaceutical glaze, povidone, sodium lauryl sulfate, starch, sucrose, and titanium dioxide. Each capsule may contain silicon dioxide.

Isometheptene Mucate, Dichloralphenazone, and Acetaminophen Capsules

Each red capsule with a pink band contains isometheptene mucate (65 mg), dichloralphenazone (100 mg), and acetaminophen (325 mg). Isometheptene mucate is a white crystalline powder that has a characteristic aromatic odor and bitter taste. It is an unsaturated aliphatic amine with sympathomimetic properties. Dichloralphenazone is a white, microcrystalline powder, with a slight odor; it tastes salty at first, and then becomes acrid. It is a mild sedative. Acetaminophen, a non-salicylate, occurs as a white, odorless, crystalline powder possessing a slightly bitter taste. Capsules contain FD&C Yellow No. 6 as a color additive.

Isosorbide Mononitrate Capsules 20 mg

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
20.00	1	Isosorbide-5-Mononitrate	20.00
60.00	2	Lactose	60.00
60.00	3	Sucrose and Cornstarch Microgranules	60.00
5.85	4	Shellac	5.85
1.20	5	Eudragit L 100	1.20
1.20	6	Eudragit RS 100	1.20
11.75	7	Talc	11.75
—	8	Alcohol	QS
—	9	Acetone	QD

MANUFACTURING DIRECTIONS

1. Charge neutral microgranules of Item 3 in a coating pan.
2. Prepare a 40% solution of shellac in alcohol, together with Item 1.
3. Maintain the temperature of microgranules at 25 ± 5°C. Apply Step 2 and dry granules, and repeat the process until all of the drug has been incorporated.
4. Sieve granules using a 1-mm aperture, and dry at 20–30°C for 8 h.
5. Prepare a 12.5% solution of equal parts of Items 5 and 6 in acetone. Spray the microgranules from Step 4 and incorporate.
6. Sieve the microgranules using a 1-mm aperture sieve.
7. Dry microgranules at 20–30°C for 8 h.
8. Spray the microgranules with balance of alcoholic shellac solution, adding talc simultaneously.
9. Adjust fill weight of granules based on assay.

Isradipine Capsules

Isradipine is a calcium antagonist available for oral administration in capsules containing 2.5 mg or 5 mg. Chemically, isradipine is 3,5-pyridinedicarboxylic acid, 4-(4-benzofurazanyl)-1,4-dihydro-2,6-dimethyl-, methyl 1-methylethyl ester. The inactive ingredients are: colloidal silicon dioxide, D&C Red No. 7 calcium lake, FD&C Red No. 40 (5 mg capsule only), FD&C Yellow No. 6 aluminum lake, gelatin, lactose, starch (corn), titanium dioxide, and other optional ingredients. The 2.5 mg and 5 mg capsules may also contain benzyl alcohol, butylparaben, edetate calcium disodium, methylparaben, propylparaben, and sodium propionate.

Itraconazole Capsules

Itraconazole, a synthetic triazole antifungal agent, is a 1:1:1:1 racemic mixture of four diastereomers (two enantiomeric pairs), each possessing three chiral centers. The capsules contain 100 mg of itraconazole coated on sugar spheres. The inactive ingredients are: gelatin, hydroxypropyl methylcellulose, polyethylene glycol (PEG) 20,000, starch, sucrose, titanium dioxide, FD&C Blue No. 1, FD&C Blue No. 2, D&C Red No. 22, and D&C Red No. 28.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
100.00	1	Itraconazole (used as pellets)	100.00
—	2	Empty Hard Gelatin Capsule, Size 0	1000
280.00	3	Sugar Spheres	280.00
32.00	4	Hydroxypropyl Cellulose	32.00
2.00	5	Polyethylene Glycol 6000	2.00
30.00	6	Cornstarch	30.00
6.00	7	Titanium Dioxide	6.00

MANUFACTURING DIRECTIONS

1. Check the assay of pellets to calculate the exact amount needed. Calculate the dose per capsule to fill.
2. Charge Items 1 and 3–7 in a suitable blender; mix for 10 min.
3. Set the capsule-filling machine with empty shells.
4. Fill the pellets as per assay.
5. Polish the capsules.

Ketoprofen and Misoprostol Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
100.00	1	Ketoprofen Delayed-Release Beads (40% Ketoprofen)	250.00
0.20	2	Misoprostol (dilute 1:100 on HPMC)	20.00
160.00	3	Lactose Anhydrous	160.00
4.00	4	Hydrogenated Vegetable Oil	4.00

MANUFACTURING DIRECTIONS

1. Item 1 beads are prepared by spray coating a suspension or solution of ketoprofen onto a nonpareil sugarcore, together with a binder (e.g., polyvinyl pyrrolidone or hydroxypropyl methylcellulose). The beads are subsequently coated with a delayed release coating (e.g., methylmethacrylate, for instance, Eudragit). Mixtures of beads with various levels of coating were used to give the required therapeutic release pattern.
   a. In a fluidized-bed apparatus, uniform spherical inert sugar cores were coated with a first layer consisting of the compounds, an inert water-soluble polymer, such as hydroxy-propylmethylcellulose or hydroxypropyl cellulose, and talc. The second layer consisted of an inert water-soluble polymer, such as hydroxypropyl methylcellulose or hydroxypropyl cellulose, talc, and a pigment, such as titanium dioxide. The third and enteric coating layer consisted of an enteric coating polymer such as co-polymerized methacrylic acid/methacrylic acid methyl esters, a plasticizer, such as triethylacetate or similar plasticizers, and talc. The layers were applied by conventional fluidized bed coating techniques using aqueous solutions or dispersions. Pseudo zero release is obtained by the use of a mixture of beads.
2. The beads in Item 1 contain 40% ketoprofen, giving a dose per capsule of 100 mg. The mix of Items 1–4 is filled into suitable hard gelatin capsules.

Ketoprofen Capsules

Ketoprofen is a nonsteroidal anti-inflammatory drug. The chemical name for ketoprofen is 2-(3-benzoylphenyl)-propionic acid. Capsules contain 25 mg, 50 mg, or 75 mg of ketoprofen for oral administration. The inactive ingredients present are: D&C Yellow No. 10, FD&C Blue No. 1, FD&C Yellow No. 6, gelatin, lactose, magnesium stearate, and titanium dioxide. The 25-mg dosage strength also contains D&C Red No. 28 and FD&C Red No. 40. Each 100 mg, 150 mg, or 200 mg capsule contains ketoprofen in the form of hundreds of coated pellets. The dissolution of the pellets is pH-dependent, with optimum dissolution occurring at pH 6.5–7.5. There is no dissolution at a pH of 1. In addition to the active ingredient, each 100 mg, 150 mg, or 200 mg capsule of Oruvail contains the following inactive ingredients: D&C Red No. 22, D&C Red No. 28, FD&C Blue No. 1, ethyl cellulose, gelatin, shellac, silicon dioxide, sodium lauryl sulfate, starch, sucrose, talc, titanium dioxide, and other optional ingredients. The 100 and 150 mg capsules also contain D&C Yellow No. 10 and FD&C Green No. 3.

Lansoprazole Capsules

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
30.00	1	Lansoprazole	30.00
93.50	2	Neutral Pellets	93.50
22.86	3	Magnesium Carbonate	22.86
66.00	4	Sucrose	66.00
37.14	5	Cornstarch	37.14
46.34	6	Hydroxypropyl Cellulose	46.34
79.68	7	Eudragit L	79.68
13.68	8	Talc	13.86
4.36	9	Titanium Dioxide	4.36
4.36	10	Polyethylene Glycol 6000	4.36
1.80	11	Polysorbate 80	1.80
—	12	Water Purified	QS

MANUFACTURING DIRECTIONS

1. Charge Items 1 and 3–5, and half of Item 6 in a suitable mixer and confirm homogeneity of mixture.
2. In a separate mixer, add and dissolve balance of Item 6 and dissolve.
3. In rotary fluid-bed dryer, charge Item 2 and incorporate Step 2 into it.
4. Prepare a suspension with Item 9 in Item 12, and Items 8, 10, and 11, and keep agitating until dissolved or well dispersed.
5. Add Item 7 and mix until well suspended.
6. Start spraying it onto the pellets from Step 3 after passing the suspension before a fine mill.
7. Fill capsules 370 mg.

Lansoprazole Delayed-Release Capsules

The active ingredient is a substituted benzimidazole, 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl] sulfinyl] benzimidazole, a compound that inhibits gastric acid secretion. Each delayed-release capsule contains enteric-coated granules consisting of lansoprazole (30 mg), hydroxypropyl cellulose, low substituted hydroxypropyl cellulose, colloidal silicon dioxide, magnesium carbonate, methacrylic acid copolymer, starch, talc, sugar sphere, sucrose, polyethylene glycol, polysorbate 80, and titanium dioxide. Components of the gelatin capsule include: gelatin, titanium dioxide, D&C Red No. 28, FD&C Blue No. 1, and FD&C Red No. 40.

Lincomycin Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
500.00	1	Lincomycin, USE Lincomycin Hydrochloride	560.00
7.00	2	Lactose	7.00
2.00	3	Aerosil 200	2.00
2.00	4	Magnesium Stearate	2.00
12.00	5	Sodium Starch Glycolate	12.00

MANUFACTURING DIRECTIONS

1. Charge all items after passing through No. 60 mesh in a low-humidity room (not more than 40%).
2. Mix for 30 min.
3. Fill 590 mg in size 0 capsules.

Linezolid Oral Suspension

Linezolid, which is a synthetic antibacterial agent of the oxazolidinone class. The chemical name for linezolid is (S)-N-[[3-[3-fluoro-4-(4-morpholinyl)phenyl]-2-oxo-5-oxazo-lidinyl]methyl]-acetamide. The oral suspension is supplied as an orange-flavored granule/powder for constitution into a suspension for oral administration. Following constitution, each 5 ml contains 100 mg of linezolid. The inactive ingredients are: sucrose, citric acid, sodium citrate, microcrystalline cellulose and carboxymethylcellulose sodium, aspartame, xanthan gum, mannitol, sodium benzoate, colloidal silicon dioxide, sodium chloride, and flavors. The sodium (Na^+) content is 8.52 mg per 5 ml (0.4 mEq per 5 ml).

Lipase, Amylase, and Protease Capsules

The pancrelipase capsules are orally administered and contain enteric-coated minitablets of porcine pancreatic enzyme concentrate, predominantly pancreatic lipase, amylase, and protease. Each capsule contains: lipase (12,000 USP units); amylase (39,000 USP units); and protease (39,000 USP units). Other combinations are 18,000/58,500/58,500 or 20,000/65,000/65,000. The capsules contain an amount of pancrelipase equivalent to but not more than 125% of the labeled lipase activity expressed in USP units. The inactive ingredients are: hydrogenated castor oil, silicon dioxide, sodium carboxymethylcellulose, magnesium stearate, microcrystalline cellulose, methacrylic acid copolymer (Type C), talc, simethicone, triethyl citrate, iron oxides, and titanium oxide.

Lithium Carbonate Capsules

Each capsule for oral administration contains lithium carbonate (150 mg, 300 mg, or 600 mg). The capsules contain talc, gelatin, FD&C Red No. 40, titanium dioxide. The imprinting ink contains FD&C Blue No. 2, FD&C Yellow No. 6, FD&C Red No. 40, synthetic black iron oxide, and pharmaceutical glaze.

Lopinavir-Ritonavir Capsules

This is a co-formulation of lopinavir and ritonavir. Lopinavir is an inhibitor of the HIV protease. As co-formulated in KALETRA®, ritonavir inhibits the CYP3A-mediated metabolism of lopinavir, thereby providing increased plasma levels of lopinavir. Lopinavir is chemically designated as [1S-[1R*,(R*),3R*,4R*]]-N-[4-[[(2,6-dimethylphenoxy)acetyl]amino]-3-hydroxy-5-phenyl-1-(phenylmethyl)pentyl]tetrahydro-alpha-(1-methylethyl)-2-oxo-1(2H)-pyrimidineacetamide. Ritonavir is chemically designated as 10-hydroxy-2-methyl-5-(1-methylethyl)-1-[2-(1-methylethyl)-4-thiazolyl]-3,6-dioxo-8,11-bis(phenylmethyl)-2,4,7,12-tetraazatridecan-13-oic acid, 5-thiazolymethyl ester, [5S-(5R*,8R*,10R*,11R*)]. Capsules are available for oral administration in a strength of 133.3 mg lopinavir and 33.3 mg ritonavir with the following inactive ingredients: FD&C Yellow No. 6, gelatin, glycerin, oleic acid, polyoxyl 35 castor oil, propylene glycol, sorbitol special, titanium dioxide, and water.

Loracarbef Capsules and Oral Suspension

Loracarbef is a synthetic (β)-lactam antibiotic of the carbacephem class for oral administration. Chemically, carbacephems differ from cephalosporin-class antibiotics in the dihydrothiazine ring where a methylene group has been substituted for a sulfur atom. The chemical name for loracarbef is: (6 *R*,7 *S*)-7-[(*R*)-2-amino-2-phenylacetamido]-3-chloro-8-oxo-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, monohydrate. Each Pulvule contains loracarbef equivalent to 200 mg (0.57 mmol) or 400 mg (1.14 mmol) anhydrous loracarbef activity. They also contain cornstarch, dimethicone, FD&C Blue No. 2, gelatin, iron oxides, magnesium stearate, titanium dioxide, and other inactive optional ingredients. After reconstitution, each 5 ml of lorabid for oral suspension contains loracarbef equivalent to 100 mg (0.286 mmol) or 200 mg (0.57 mmol) anhydrous loracarbef activity. The suspensions also contain cellulose, FD&C Red No. 40, flavors, methylparaben, propylparaben, simethicone emulsion, sodium carboxymethylcellulose, sucrose, and xanthan gum.

Loxapine Capsules

Loxapine, a dibenzoxazepine compound, represents a subclass of tricyclic antipsychotic agents, chemically distinct from the thioxanthenes, butyrophenones, and phenothiazines. Chemically, it is 2-chloro-11-(4-methyl-1-piperazinyl)dibenz[b,f][1,4]oxazepine. It is present as the succinate salt. Each capsule, for oral administration, contains loxapine succinate (6.8, 13.6, 34.0, or 68.1 mg) equivalent to 5, 10, 25, or 50 mg of loxapine base, respectively. It also contains the following inactive ingredients: gelatin, silicon dioxide, sodium lauryl sulfate, anhydrous lactose, D&C Yellow No. 10, FD&C Blue No. 1, polacrilin potassium, magnesium stearate, talc, and titanium dioxide. Additionally, the 5-mg capsule contains D&C Red No. 33, the 10-mg capsule contains D&C Red No. 28 and D&C Red No. 33, and the 25-mg capsule contains FD&C Yellow No. 6.

Loxapine Succinate Capsules

Loxapine, a dibenzoxazepine compound, represents a subclass of tricyclic antipsychotic agents, chemically distinct from the thioxanthenes, butyrophenones, and phenothiazines. Chemically, it is 2-chloro-11-(4-methyl-1-piperazinyl)dibenz[b,f][1,4]oxazepine. It is present as the succinate salt. Each capsule for oral administration contains loxapine succinate 6.8, 13.6, 34.0, or 68.1 mg equivalent to 5, 10, 25, or 50 mg of loxapine base, respectively. It also contains the following inactive ingredients: gelatin, silicon dioxide, sodium lauryl sulfate, anhydrous lactose, D&C Yellow No. 10, FD&C Blue No. 1, polacrilin potassium, magnesium stearate, talc, and titanium dioxide. Additionally, the 5-mg capsule contains D&C Red No. 33, the 10 mg capsule contains D&C Red No. 28 and D&C Red No. 33, and the 25 mg capsule contains FD&C Yellow No. 6.

Magaldrate Instant Powder or Dry Syrup

Bill of Materials			
Scale (mg/Sachet)	**Item**	**Material Name**	**Qty/1000 Sachets (g)**
800.00	1	Magaldrate	800.00
640.00	2	Kollidon CL-M	640.00
200.00	3	Sorbitol, Crystalline	200.00
40.00	4	Orange Flavor	40.00
40.00	5	Kollidon 90 F	40.00
4.00	6	Coconut Flavor	4.00
4.00	7	Banana Flavor	4.00
0.80	8	Saccharin Sodium	0.80
QS	9	Water	about 280 ml

MANUFACTURING DIRECTIONS

1. Granulate a mixture of Items 1–4 with solution of Items 5–9, and pass through a 0.8-mm sieve to obtain free-flowing granules.
2. Fill 2 g in sachets or 20 g in a 100-ml flask. For instant granules in sachets: suspend 2 g (= 1 sachet) in a glass of water (= 800 mg magaldrate).

Magnesium Oxide Capsules

Each capsule contains magnesium oxide (140 mg USP [Heavy]) or 84.5 mg of elemental magnesium (6.93 mEq).

Mefenamic Acid Capsules

Mefenamic acid is a member of the fenamate group of nonsteroidal anti-inflammatory drugs (NSAIDs). Each blue-banded, ivory capsule contains 250 mg of mefenamic acid for oral administration. Each capsule also contains lactose. The capsule shell and band contain citric acid, D&C Yellow No. 10, FD&C Blue No. 1, FD&C Red No. 3, FD&C Yellow No. 6, gelatin, glycerol monooleate, silicon dioxide, sodium benzoate, sodium lauryl sulfate, and titanium dioxide.

Mesalamine Capsules

Mesalamine for oral administration is a controlled-release formulation of mesalamine, an aminosalicylate anti-inflammatory agent for gastrointestinal use. Chemically, mesalamine is 5-amino-2-hydroxybenzoic acid. Each capsule contains 250 mg of mesalamine. It also contains the following inactive ingredients: acetylated monoglyceride, castor oil, colloidal silicon dioxide, ethylcellulose, hydroxypropyl methylcellulose, starch, stearic acid, sugar, talc, and white wax. The capsule shell contains D&C Yellow No. 10, FD&C Blue No. 1, FD&C Green No. 3, gelatin, titanium dioxide, and other optional ingredients.

Mesalamine Colonic Delivery Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
250.00	1	Mesalamine (5-ASA)	250.00
45.00	2	Lactose	45.00
5.20	3	Polyvinylpyrrolidone	5.20
10.80	4	Sodium Starch Glycolate	10.80
3.60	5	Magnesium Stearate	3.60
36.80	6	Talc	36.80
18.40	7	Eudragit S100	18.40
43.20	8	Eudragit NE 30D	43.20
0.40	9	Antifoam Emulsion SE 2	0.40

MANUFACTURING DIRECTIONS

1. Add Items 1 and 2 to a blending vessel; mix well.
2. Add Item 4 and blend.
3. Prepare an aqueous solution of Item 3, and granulate Step 2.
4. Dry and compress; reduce size by passing through 0.5–1.2-mm sieve.
5. The granules in Step 4 are loaded into a fluid-bed coater and then spray-coated with an aqueous suspension to provide a 20% or 25% dry weight gain based on an uncoated granule weight of a mixture of Eudragit S100 and Eudragit NE 30D (Rohm Pharma GmbH, Darmstadt, Germany) in the ratio of 3:7. Eudragit S100 is a copolymer of methacrylic acid and methylmethacrylate in the ratio of 1:2 in powder form and Eudragit NE 30D is a 30% aqueous dispersion of a copolymer of ethylacrylate and methylmethacrylate in the ratio 2:1.
6. Coated granules are packed into size 00 hard gelatin capsules in an amount of 400 mg granules per capsule.

   The capsules are then spray-coated with a coating solution of the following formula:

   Eudragit L powder, 3 g
   Diethyl phthalate, 0.75 ml
   Silicone fluid 200 cs, 0.75 ml
   Acetone, 100 ml

Methsuximide Capsules

Methsuximide is an anticonvulsant succinimide, chemically designated as *N*,2-dimethyl-2-phenylsuccinimide. Each capsule contains 150 mg or 300 mg methsuximide, as well as starch. The capsule contains colloidal silicon dioxide, D&C Yellow No. 10, FD&C Yellow No. 6, gelatin, and sodium lauryl sulfate.

Methylphenidate Capsules

Methylphenidate is a central nervous system (CNS) stimulant. Chemically, methylphenidate HCl is *d,l* racemic *threo*-methyl(alpha)-phenyl-2-piperidineacetate hydrochloride. It contains 20 mg of methylphenidate hydrochloride for oral administration. The extended-release capsules comprise both immediate-release (IR) and extended-release (ER) beads such that 30% of the dose (6 mg) is provided by the IR component, and 70% of the dose (14 mg) is provided by the ER component. It also contains the following inert ingredients: sugar spheres, povidone, hydroxypropyl methylcellulose and polyethylene glycol, ethylcellulose aqueous dispersion, dibutyl sebacate, gelatin, titanium dioxide, and FD&C Blue No. 2.

MANUFACTURING DIRECTIONS

1. Methylphenidate HCl (200 g) is slowly added to an aqueous solution (about 15% solids) of polyvinylpyrrolidone (10 g Povidone K-30) and mixed well.
2. About 25–30 mesh sugar spheres (770 g) were coated with the drug solution in a fluid-bed granulator. The drug-containing pellets are dried, and a sealcoat of Opadry Clear® (20 g) is first applied to produce instant-release or IR beads.
3. Extended-release (ER) beads are produced by taking IR beads and coating with the dissolution rate controlling polymer. A plasticized ethylcellulose coating is applied to the methylphenidate particles (893 g) by spraying Aquacoat ECD-30® (233 g) and dibutyl sebacate (16.8 g).
4. An outer seal coating formulation (20 g) of Opadry® is sprayed onto the coated active particles. The coated particles are cured at 60°C for 12 h so that polymer particles coalesce to form a smooth membrane on ER beads. The instant-release (IR) and ER beads are then filled into hard gelatin capsules with dual bead-filling hoppers.

Methylphenidate Immediate- and Extended-Release Capsules

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
25.00	1	Methylphenidate	25.00
1.25	2	Polyvinylpyrrolidone K-30	1.25
96.25	3	Sugar Spheres 25–30 Mesh	96.25
2.25	4	Opadry Clear	2.25
29.12	5	Aquacoat ECD-30	29.12
2.10	6	Dibutyl Sebacate	2.10
2.25	7	Opadry Clear	2.25
—	8	Alcohol	QS

MANUFACTURING DIRECTIONS

1. This product consists of two types of beads: instant release and extended release. The extended release beads are formed by further coating of instant release beads.
2. Instant release beads are produced by preparing a 15% solution of Item 2 in Item 8 and adding Item 1 to it slowly.
3. Charge Item 3 in a fluid-bed granulator, and load drug solution in Step 2 onto sugar pellets. Dry and apply seal coat of Item 4. This completes the process of preparing instant release beads.
4. Take an appropriate quantity (893 g) of beads in Step 3 and apply a coating of Item 6 in Item 8.
5. Apply Item 7 seal coat (as 15% aqueous solution), and cure at 60°C for 12 h for polymer particles to coalesce into a uniform film.
6. Fill in gelatin capsules using a 20:80, 30:70, or 40:60 mixture of instant release to extended release beads. Use equipment that is capable of filling beads simultaneously.

Methyltestosterone Capsules

Methyltestosterone, a synthetic derivative of testosterone, is an androgenic preparation given by the oral route in a capsule form. Each capsule contains 10 mg of methyltestosterone. Each capsule, for oral administration, contains 10 mg of methyltestosterone. In addition, each capsule contains the following inactive ingredients: cornstarch, gelatin, FD&C Blue No. 1, FD&C Red No. 40. Each capsule also contains the following inactive ingredients: cornstarch, gelatin, FD&C Blue No. 1, and FD&C Red No. 40.

Metoclopramide Hydrochloride Sustained-Release Capsules

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
20.00	1	Metoclopramide, USE Metoclopramide Hydrochloride	21.00
183.90	2	Sucrose and Cornstarch Microgranules, Size 20	183.90
0.12	3	Disodium Edetate	0.12
0.19	4	Stearic Acid	0.19
1.30	5	Methacrylic Acid Copolymer Eudragit L100	1.30
0.42	6	Cornstarch	0.42
9.07	7	Shellac, bleached wax-free	9.07
15.00	8	Talc	15.00
1.00	9	Gelatin Capsules, Size 3	1000.00
—	10	Alcohol	QS
—	11	Water Purified	11.00

MANUFACTURING DIRECTIONS

1. The neutral microgranules (Item 2) are placed in an appropriate coating pan, and the pan is rotated.
2. In a separate vessel, prepare an alcoholic solution of Item 5. Spray in Step 1.
3. Prepare alcohol solution of Item 4 in alcohol, and spray into Step 2.
4. Prepare aqueous solution of Item 3, and spray into Step 3.
5. Mix Item 1 with Item 6, and add to Step 4 alternating with an alcoholic solution of Eudragit until all of the drug has been incorporated.
6. Sieve the microgranules.
7. Apply aqueous solution of Item 3 followed by an alcohol solution of Eudragit L and microgranules dried.
8. Apply alcoholic solution of shellac alternating with talc until all shellac solution is used.
9. Lubricate and fill in capsules; sieve and dry microgranules.

Metyrosine Capsules

Metyrosine is (-)-(α)-methyl-*L*-tyrosine or (α)-MPT. It is supplied as capsules for oral administration. Each capsule contains 250 mg of metyrosine. The inactive ingredients are: colloidal silicon dioxide, gelatin, hydroxypropyl cellulose, magnesium stearate, and titanium dioxide. The capsules may also contain any combination of D&C Red No. 33, D&C Yellow No. 10, FD&C Blue No. 1, and FD&C Blue No. 2.

Miconazole Nitrate Foot and Itch Powder

Spray powder for athlete's foot contains miconazole nitrate 2%. It also contains alcohol SD-40 (10% w/w), isobutane, starch/acrylates/acrylamide copolymer, stearalkonium hectorite, and talc. Spray powder for jock itch contains miconazole nitrate 2%. It also contains alcohol SD-40 (10% w/w), isobutane, stearalkonium hectorite, and talc. Spray deodorant powder contains miconazole nitrate 2%. It also contains isobutane, alcohol SD-40 (10% w/w), talc, starch/acrylates/acrylamide copolymer, stearalkonium hectorite, and fragrance. Powder contains miconazole nitrate 2%. It also contains benzethonium chloride, cornstarch, kaolin, sodium bicarbonate, starch/acrylates/acrylamide copolymer, and zinc oxide.

Mineral Powder for Topical Herpes Simplex

Bill of Materials			
Scale (mg/g)	**Item**	**Material Name**	**Qty/kg (g)**
14.00	1	Calcium Carbonate	14.00
14.00	2	Sodium Carbonate	14.00
14.00	3	Sodium Dihydrogen Phosphate Anhydrous	14.00
80.00	4	Calcium Hypochlorite	80.00
818.00	5	Cornstarch	818.00

MANUFACTURING DIRECTIONS

1. Mix all ingredients after passing through an 80-mesh screen.
2. Pack in bottles.

Minocycline Hydrochloride Capsules

Minocycline hydrochloride, a semisynthetic derivative of tetracycline, is [4*S*-(4(alpha),4a(alpha),5a(alpha),12a(alpha))]-4,7-bis(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11-dioxo-2-naphthacenecarboxamide monohydrochloride. Each minocycline hydrochloride capsule for oral administration contains the equivalent of 50 mg, 75 mg, or 100 mg of minocycline. In addition, each capsule contains the following inactive ingredients: magnesium stearate and starch (corn). The 50-mg, 75-mg, and 100-mg capsule shells contain gelatin, silicon dioxide, sodium lauryl sulfate, and titanium dioxide. The 75-mg and 100-mg capsule shells also contains black iron oxide.

Mixed Amphetamine Salt Capsules

It is a once daily extended-release, single-entity amphetamine product. It combines the neutral sulfate salts of dextroamphetamine and amphetamine, with the dextro isomer of amphetamine saccharate and *d*,*l*-amphetamine aspartate monohydrate. The capsule contains two types of drug-containing beads designed to give a double-pulsed delivery of amphetamines, which prolongs the release of amphetamine compared to the conventional immediate-release tablet formulation. Each capsule contains equal quantities of four salts of amphetamine to give a total of 10, 20, or 30 mg of content (total amphetamine base equivalence of 6.3, 12.5, and 18.8 mg): dextroamphetamine saccharate, amphetamine aspartate monohydrate, dextroamphetamine sulfate, amphetamine sulfate. The inactive ingredients in the capsules include: gelatin capsules, hydroxypropyl methylcellulose, methacrylic acid copolymer, Opadry beige, sugar spheres, talc, and triethyl citrate. The gelatin capsules contain edible inks, kosher gelatin, and titanium dioxide. The 10-mg capsules also contain FD&C Blue No. 2. The 20-mg and 30-mg capsules also contain red iron oxide and yellow iron oxide.

Mixed Amphetamine Salts Enteric-Release Capsules

Bill of Materials

Item	Material Name	Qty/kg (g)
	Immediate-Release Beads	
1	Amphetamine Mixed Salts[a]	88.00
2	Nonpareil Seeds (30/35 Mesh, Paulaur)	6.80
3	Hydroxypropyl Methylcellulose E5 Premium	0.60
4	Water Purified	QS
	Enteric-Release Pellets	
5	Immediate-Release Beads (see Items 1–4)	40.00
6	Eudragit L30-D-55	24.88
7	Triethyl Citrate	2.52
8	Talc	2.60
9	Water Purified	QS

[a] Mixed salts include: amphetamine sulfate, amphetamine aspartate, and dixtroamphetamine sulfate.

MANUFACTURING DIRECTIONS

1. Charge Item 2 in a fluid-bed processor, and fluidize at 60°C.
2. Prepare a suspension of Item 3 (prepare a 1% solution) and Item 1 using Item 4; assure it is free of agglomerates and contains no fines, with a yield of at least 98%.
3. Apply binder solution to Step 1, and load the drug.
4. Charge Item 5 into a fluid-bed processor.
5. Prepare the coating dispersion using Items 6–8 in Item 9, and mix for at least 30 min.
6. Spray the coating solution in Step 5 onto Step 1 until a target level of 20 µm is achieved.
7. Dry pellets at 30–35°C for 5 min before stopping the processor.
8. Fill to contain in each capsule base equivalent, 10 mg, 20 mg, and 30 mg (Adderall XR®).

Morphine Sulfate Capsules

Chemically, morphine sulfate is 7,8didehydro-4,5(alpha)-epoxy-17-methylmorphinan-3,6(alpha)-diolsulfate(2:1)(salt)pentahydrate. Each capsule for oral administration contains morphine sulfate 15 or 30 mg. The inactive ingredients are: FD&C Blue No. 1, FD&C Blue No. 2, FD&C Red No. 40, FD&C Yellow No. 6, gelatin, hydroxypropyl methylcellulose, lactose, polyethylene glycol, polysorbate 80, polyvinylpyrrolidone, starch, sucrose, titanium dioxide, and other optional ingredients. In addition, the 30-mg capsule contains black iron oxide and D&C Red No. 28.

Morphine Sulfate Controlled-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
40.00	1	Morphine Hydrochloride	40.00
40.00	2	Lactose	40.00
20.00	3	Microcrystalline Cellulose	20.00
QS	4	Water Purified	QS
3.50–5.30	5	Ethyl Cellulose	3.50–5.30
2.20–3.40	6	Hydroxypropyl Methylcellulose	2.20–3.40
0.60–1.0	7	Triethyl Citrate	0.60–1.00
QS	8	Ethanol	QS
QS	9	Methyl Isobutyl Ketone	QS

MANUFACTURING DIRECTIONS

1. Mixing and Granulating: Morphine hydrochloride (40% w/w), lactose (40% w/w), and microcrystalline cellulose (Avicel PH-101) (20% w/w) totally 1500 gram are dry-mixed in a planetary type mixer (Kenwood Major®) at a low mixing speed (speed adjustment < 1) for 10 min. Water (585 g) is added and the mass is granulated for 5 min at speed adjustment 2.
2. Extrusion: Extrusion is performed in a Nica™ E-140 Extruder (Lejus Medical AB, Sweden) through a perforated screen with drilled orifices of 1.0 mm in diameter. The speed of the agitator and the feeder is set on the lowest values.
3. Spheronization: Spheronization is conducted in a mammerizer (Ferro Mecano AB, Sweden). The speed of the Marumerizer™ plate is adjusted to 450 rpm. The number of spheronization rounds is 5, with about 400 g of wet extrudates on the plates at each run.
4. Drying: Drying is performed in a fluid bed dryer (Aeromatic AG®, West Germany) at an IN-temperature of 50°C. The batch is divided into sub-batches of 600–700 g wet particulate cores. Each sub-batch is dried for 5 min at the air velocity adjustment 20 in order to obtain individual cores rather than aggregates. The sub-batches are then mixed and the whole batch is dried at adjustment 12 for 65 min. The end OUT-temperature is 36°C. The yield of dry cores after drying is 1437 g and 96% w/w.
5. Sieving: Sieving is performed by using analytical sieves with sieve sizes of 0.71 mm and 1.40 mm, respectively. The yield of dry cores after sieving is 1337 gram and 89% w/w. The yields are 96% and 89% w/w after drying and sieving, respectively.
6. A sieving analysis before and after abrasion of the cores shows that about 93% of the cores have a size between 0.71 and 1.0 mm. A crushing strength analysis shows that the mean crushing strength of 1.0-mm particles is 4.71 N. A hardness value at this level makes it possible to coat the particles in small as well as in large equipment.
7. Morphine hydrochloride cores manufactured as above are coated with controlled-release membranes. Hydroxypropyl methylcellulose (HPMC) (E5) and ethyl cellulose (EC) (10 cps) were used as film formers together with triethyl citrate (TEC) as a plasticizer. The coating solution contains 99.5% ethanol and methyl isobutyl ketone (MIBK).
8. The coating is performed using a spray coating equipment (Nica™ FB-coater, Sweden). The spray gun used is a Binks & Bullows with a J92R liquid nozzle and a J930 air nozzle. A net device is placed in the top of the fluidized bed to avoid loss of cores to the cyclone output. The spray gun is mounted on a height over the bottom of the bed for 185 min. Ethanol/MIBK mixture is pumped through the system before to the start of the coating, and there is consequently liquid present between the pump housing and the spray gun. The morphine hydrochloride cores prepared above are loaded. The cores are preheated at 55°C with an air velocity of 20–25 m^3/h for 4 min. At the start of the coating, the bed temperature is 32–36°C. The coating is started using the following process parameters: atomizing pressure 500 kPa, air velocity 85 m^3/h, and a solution flow of about 24 ml/min. The registered IN-temperature varies between 53–56°C, and the OUT-temperature varies between 34–38°C during the coating.

9. The coated spheres are sieved through a 1.4 mm-sieve, and spheres with a size less than 1.4 mm are collected.
10. The collected spheres are filled into hard gelatin capsules (hard gelatin capsule, color white, No. 2) with a normal weight of 0.17 g (net weight 108 mg). The mean content of active component in the capsules is between 36 and 44 mg.

Morphine Sulfate Sustained-Release Capsules

Each sustained-release capsule contains either 20, 30, 50, 60, or 100 mg of morphine sulfate and the following inactive ingredients that are common to all strengths: hydroxypropyl methylcellulose, ethylcellulose, methacrylic acid copolymer, polyethylene glycol, diethyl phthalate, talc, cornstarch, and sucrose. The 20-mg capsule shell contains gelatin, silicon dioxide, sodium lauryl sulfate, D&C Yellow No. 10, titanium dioxide, and black ink (SW-9009). The 30-mg capsule shell contains gelatin, silicon dioxide, sodium lauryl sulfate, FD&C Red No. 3, FD&C Blue No. 1, titanium dioxide, and black ink (S-1-8114 or S-1-8115). The 50-mg capsule shell contains gelatin, silicon dioxide, sodium lauryl sulfate, D&C Red No. 28, FD&C Red No. 40, FD&C Blue No. 1, titanium dioxide, and black ink (SW-9009). The 60-mg capsule shell contains gelatin, silicon dioxide, sodium lauryl sulfate, D&C Red No. 28, FD&C Red No. 40, FD&C Blue No. 1, titanium dioxide, and black ink (S-1-8114 or S-1-8115). The 100-mg capsule shell contains gelatin, silicon dioxide, sodium lauryl sulfate, D&C Yellow No. 10, FD&C Blue No. 1, titanium dioxide, and black ink (SW-9009).

Multivitamin Effervescent Granules

Bill of Materials			
Scale (mg/Sachet)	**Item**	**Material Name**	**Qty/1000 Tabs (g)**
2.600	1	Thiamin Hydrochloride (BASF)	0.26
3.000	2	Riboflavin (BASF)	0.30
11.000	3	Nicotinamide	1.10
2.500	4	Pyridoxine Hydrochloride (BASF)	0.25
15.000	5	Calcium D-Pantothenate (BASF)	1.50
200.000	6	Ascorbic Acid Powder (BASF)	20.00
500.000	7	Citric Acid	50.00
1300.000	8	Sucrose	130.00
800.000	9	Fructose	80.00
200.000	10	Kollidon CL-M	20.00
250.000	11	Flavors	25.00
20.000	12	Cyclamate Sodium	2.00
1.000	13	Saccharine Sodium	0.10
150.000	14	Kollidon VA 64	15.00
350.000	15	Isopropanol	35.00
15.000	16	Vitamin A Acetate Dry Powder 325,000 IU/g CWD (BASF)	1.50
8.000	17	Vitamin D3 Dry Powder 100,000 IU/g CWD (BASF)	0.80
21.000	18	Vitamin E Acetate Dry Powder 50%	2.10
0.066	19	Cyanocobalamin Gelatin Coated 0.1% (BASF)	0.66
400.000	20	Sodium Bicarbonate	40.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of Items 1–13 with solution of Items 14 and 15; pass through a 0.8-mm sieve, dry well, and mix with Items 16–20.
2. Fill 4 g in sachets.

Multivitamin Instant Granules

Bill of Materials			
Scale (mg/6 g Sachet)	**Item**	**Material Name**	**Qty/30 kg (g)**
40.00	1	Vitamin A+D dry powder + 50,000 IU/g CWD (BASF)	200.00
5.00	2	Thiamine Mononitrate (BASF)	26.00
6.00	3	Riboflavin (BASF)	33.00
22.00	4	Nicotinamide	110.00
4.50	5	Pyridoxine Hydrochloride (BASF)	22.00
30.00	6	Calcium D-Pantothenate (BASF)	150.00
0.013	7	Cyanocobalamin, USE Cyanocobalamin 0.1% Gelatin Coated (BASF)	66.00
230.00	8	Ascorbic Acid Powder (BASF)	1150.00
42.00	9	Vitamin E Acetate Dry Powder	210.00
4000.00	10	Sucrose, finely ground	20,000.00
1000.00	11	Kollidon CL-M	5000.00
200.00	12	Orange Flavor	1000.00
400.00	13	Kollidon VA 64	2000.00
—	14	Ethanol or Isopropanol	Approx. 7 l

MANUFACTURING DIRECTIONS

1. Pass mixture through a 0.8-mm sieve, and granulate with solution of Items 13 and 14 in the fluidized bed. Fill the granules in sachets. If the technology of a fluidized bed is not available, the dry powders of vitamin A, E, and B12 should be added after the granulation of the other components. Suspend 6–12 g (= 1 sachet) in a glass of water corresponding to 2–4 RDA of vitamins. Double-strength sachet filled at 12 g.

Mycophenolate Mofetil Capsules and Oral Suspension

Mycophenolate mofetil is the 2-morpholinoethyl ester of mycophenolic acid (MPA), an immunosuppressive agent; inosine monophosphate dehydrogenase (IMPDH) inhibitor. The chemical name for mycophenolate mofetil (MMF) is 2-morpholinoethyl (E)-6-(1,3-dihydro-4-hydroxy-6-methoxy-7-methyl-3-oxo-5-isobenzofuranyl)-4-methyl-4-hexenoate. The inactive ingredients in 250-mg capsules include: croscarmellose sodium, magnesium stearate, povidone (K-90), and pregelatinized starch. The capsule shells contain black iron oxide, FD&C Blue No. 2, gelatin, red iron oxide, silicon dioxide, sodium lauryl sulfate, titanium dioxide, and yellow iron oxide. The inactive ingredients in CellCept oral suspension include: aspartame, citric acid anhydrous, colloidal silicon dioxide, methylparaben, mixed fruit flavor, sodium citrate dihydrate, sorbitol, soybean lecithin, and xanthan gum.

Nanoparticle Polymer Particle Powders

1. Preparation of Polymer Nanoparticles of Ketorolac: To 900 mg NIPAAM (N-isopropyl is acrylamide), 100 ml freshly distilled VP (vinyl pyrrolidone), and 50 ml freshly distilled AA (acrylic acid) in 100 ml of water, 300 ml MBA (methylene bis acrylamide) ([MBA] = 0.049 gm/ml) is added to cross-link the polymer chain. The dissolved oxygen is removed by passing nitrogen gas for 30 min; 50 ml of 0.5% w/v ferrous ammonium sulphate (FAS) and 50 ml saturated ammonium persulphate (APS) solutions are then added to initiate the polymerization reaction. The polymerization is done at 30°C, for 24 h in nitrogen atmosphere. Total aqueous solution of polymer is then dialyzed overnight using a spectrapore membrane dialysis bag (12 kD cut off). The dialyzed aqueous solution of polymeric micelles is frozen in liquid nitrogen and is lyophilized immediately to obtain dry powder for subsequent use. The yield of micelle nanoparticles is more than 80%. The lyophilized powder is easily redispersible in aqueous buffer; 100 mg of lyophilized powder of polymeric micelles is dispersed in 10 ml of water and is stirred well to disperse the micelles. The free acid form of ketorolac is dissolved in absolute ethanol ([ketorolac] = 50 mg/ml) and the alcoholic solution is added in polymeric micelles slowly with constant stirring. Ketorolac got directly loaded into hydrophobic core of micelles. The drug-loaded polymeric micelles are then lyophilized to get dry powder for subsequent use.
2. Preparation of Polymeric Nanoparticles Containing Indomethacin: In 100 mg of the lyophilized powder of the polymeric micelle nanoparticles, an alcoholic solution of indomethacin ([indomethacin] = 33 mg/ml) is added with constant stirring to get clear solution of polymeric micelles containing the drug of desired concentration dispersed in aqueous buffer. Maximum 10% w/w of the drug can be dissolved in polymeric micelles at room temperature. The drug-loaded polymeric micelles are then lyophilized to get dry powder for subsequent use.
3. Preparation of Polymeric Micelles Containing Nimesulide: In 100 mg of dry powder of polymeric micelles, an alcoholic solution of nimesulide ([nimesulide] = 10 mg/ml) is added with constant stirring to get a clear solution. Maximum 8% w/w of nimesulide could be dissolved in polymeric micelles at room temperature. The drug-loaded micelles are then lyophilized to get dry powder for subsequent use.

Nelfinavir Mesylate Oral Powder

Nelfinavir mesylate is an inhibitor of the human immunodeficiency virus (HIV) protease. Oral powder is available for oral administration in a 50 mg/g strength (as nelfinavir freebase) in bottles. The oral powder also contains the following inactive ingredients: microcrystalline cellulose, maltodextrin, dibasic potassium phosphate, crospovidone, hydroxypropyl methylcellulose, aspartame, sucrose palmitate, and natural and artificial flavors. The chemical name for nelfinavir mesylate is [3 *S*-[2(2 *S**, 3 *S**), 3(alpha),4a(beta),8a(beta)]]-N-(1,1-dimethylethyl)decahydro-2-[2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-3-isoquinolinecarboxamide monomethanesulfonate (salt) and the molecular weight is 663.90 (567.79 as the freebase).

Bill of Materials

Scale (mg/g)	Item	Material Name	Qty/kg (g)
50.00	1	Nelfinavir Mesylate	50.00
50.00	2	Sodium Carboxymethylcellulose	50.00
1.25 ml	3	Syrup	1.25 l
0.10 ml	4	Benzoic Acid Solution	0.10 l
QS	5	Flavor	QS
QS	6	Dye	QS
QS to 5 ml	7	Purfied Water	5 l

MANUFACTURING DIRECTIONS

The active ingredient is passed through a No. 45-mesh sieve and mixed with the sodium carboxymethylcellulose and syrup to form a smooth paste. The benzoic acid solution, flavor, and color are diluted with a portion of the water and added, with stirring. Sufficient water is then added to produce the required volume.

Nilvadipine Capsules

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
14.00	1	Nilvadipine	14.00
166.00	2	Polyethylene Glycol 400	166.00
20.00	3	Hydroxypropyl Methylcellulose	10.00

MANUFACTURING DIRECTIONS

1. Add and dissolve Item 1 in Item 2.
2. Add Item 3, and fill 200 mg in a size 4 hard gelatin capsule.

Nitrofurantoin Capsules

A nitrofurantoin macrocrystal is a synthetic chemical of controlled crystal size. Inactive ingredients: Each capsule contains edible black ink, gelatin, lactose, starch, talc, titanium dioxide, and may contain FD&C Yellow No. 6 and D&C Yellow No. 10. Nitrofurantoin is an antibacterial agent specific for urinary tract infections. Another formulation of nitrofurantoin capsule is a hard gelatin capsule shell containing the equivalent of 100 mg of nitrofurantoin in the form of 25 mg of nitrofurantoin macrocrystals and 75 mg of nitrofurantoin monohydrate. Inactive ingredients: Each capsule contains carbomer 934P, cornstarch, compressible sugar, D&C Yellow No. 10, edible gray ink, FD&C Blue No. 1, FD&C Red No. 40, gelatin, lactose, magnesium stearate, povidone, talc, and titanium dioxide.

Nitrofurantoin Sustained-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
150.00	1	Nitrofurantoin Monohydrate (Norwich Eaton Pharmaceuticals, Inc.)	150.00
17.70	2	Carbopol 934P (B.F. Goodrich)	17.70
181.00	3	PVP C-15 (GAF Corporation)	181.00
3.50	4	Talc	3.50
1.80	5	Zinc Stearate	1.80

MANUFACTURING DIRECTIONS

1. The Carbopol 934P, PVP C-15 (mean molecular weight of about 8000, talc, and zinc stearate are combined in a mortar and triturated well.
2. The nitrofurantoin monohydrate is added to this mixture in the mortar and triturated well until a substantially uniform particulate mixture is achieved.
3. The resulting particulate mixture (354 mg) is filled into size 1 hard gelatin capsule shells.

Nizatidine Capsules

Nizatidine is a histamine H2-receptor antagonist. Chemically, it is N-[2-[[[2-[(dimethylamino)methyl]-4-thiazolyl]methyl]thio]ethyl]-N′-methyl-2-nitro-1,1-ethenediamine. Each capsule contains pregelatinized starch, dimethicone, starch, titanium dioxide, yellow iron oxide, 150 mg (0.45 mmol) or 300 mg (0.91 mmol) of nizatidine, and other inactive ingredients. The 150-mg capsule also contains magnesium stearate, and the 300-mg capsule also contains croscarmellose sodium, povidone, red iron oxide, and talc.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
150.00	1	Nizatidine	150.00
33.70	2	Cornstarch	33.70
15.00	3	Pregelatinized Starch (Starch 1500)	15.00
0.70	4	Magnesium Stearate	0.70
0.60	5	Simethicone	0.60
	6	Empty Hard Gelatin Shell, Size 2 (Bovine Origin)	1000

MANUFACTURING DIRECTIONS

1. Add and blend Items 1–3 in a suitable blender, and mix for 20 min.
2. Add Item 4 and blend for 10 min
3. Add Item 5 and blend for 4 min.
4. Fill in 200 mg of hard gelatin capsules.

Nystatin Powder

Nystatin is a polyene antifungal antibiotic obtained from *Streptomyces noursei.* Nystatin Topical Powder is for dermatologic use and contains 100,000 USP nystatin units per gram dispersed in talc.

Omeprazole and Piroxicam Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
95.70	1	Omeprazole Enteric-Coated Pellets	95.70
122.70	2	Piroxicam Enteric-Coated Pellets	122.70

MANUFACTURING DIRECTIONS

1. This product requires preparation of enteric coated pellets of omeprazole and piroxicam separately.
2. The omeprazole pellets are prepared by applying drug solution (in HPMC) on non-pareil sugar beads, applying a separating layer consisting of HPMC alone and then applying an enteric coating that comprises methylacrylic acid copolymer 30% suspension with triethyl citrate, mono-, and diglycerides and polysorbate 80 in purified water. Finally an overcoat is applied.
   - Core material (omeprazole)
     - Magnesium omeprazole: 5.00 kg
     - Nonpareil cores: 10.00 kg
     - Hydroxypropyl methylcellulose: 0.75 kg
     - Water purified: 19.65 kg
   - Separating layer (omeprazole)
     - Core material (acc. to above): 14.60 kg
     - Hydroxypropyl cellulose: 1.46 kg
     - Talc: 2.5 kg
     - Magnesium stearate: 0.21 kg
     - Water purified: 29.2 kg
   - Enteric coating layer (omeprazole)
     - Pellets with separate layer (acc. to above): 9.00 kg
     - Methacrylic acid copolymer (30% suspension): 15.00 kg
     - Triethyl citrate: 1.35 kg
     - Mono- and diglycerides: 0.22 kg
     - Polysorbate 80: 0.02 kg
     - Water purified: 8.8 kg
   - Over-coating layer (omeprazole)
     - Enteric coating layered pellets: 9.0 kg
     - Hydroxypropyl methylcellulose: 0.18 kg
     - Mg-Stearate: 0.005 kg
     - Water purified: 3.6 kg
3. The piroxicam pellets are prepared by a similar method except using a hydro-alcoholic solution in the first instance, not using a separating layer and performing enteric coating using HPMC succinate.
   - Core material (piroxicam)
     - Piroxicam micronized: 35 g
     - Sugar seeds: 100 g
     - Hydroxypropyl methylcellulose: 6 cps, 25 g
     - Water purified: 250 g
     - Ethanol 99% (w/v): 250 g
   - Enteric coating layer (piroxicam)
     - Piroxicam pellets (acc. to above): 100 g
     - Hydroxypropyl methylcellulose acetate-succinate: 14.38 parts
     - Triethyl citrate: 2.87 parts
     - Sodium lauryl sulphate: 0.43 parts
     - Talc: 4.32 parts
     - Water purified: 183.3 parts
4. Coat with a suspension of the preceding composition to give a product with a content of 163 mg/g; suspension layering is performed in a fluid bed equipment. Micronized piroxicam is sprayed onto inert non-pareil cores from a water suspension containing the dissolved binder.

Omeprazole Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
40.00	1	Omeprazole	40.00
68.00	2	Sucrose and Cornstarch Neutral Microgranules, Size 26	68.00
4.00	3	Sodium Starch Glycollate (Explotab)	4.00
6.00	4	Sodium Lauryl Sulfate	6.00
7.12	5	Polyvidone	7.00
5.96	6	Hydroxypropyl Methylcellulose	5.96
36.15	7	Eudragit L30D	36.15
3.62	8	Triethyl Citrate	3.62
15.40	9	Talc	15.40
—	10	Alcohol	QS

Omeprazole Delayed-Release Capsules

The active ingredient in omeprazole delayed-release capsules is a substituted benzimidazole, 5-methoxy-2-[[(4-methoxy-3, 5-dimethyl-2-pyridinyl) methyl]sulfinyl]-1 *H*-benzimidazole, a compound that inhibits gastric acid secretion. Each delayed-release capsule contains either 10 mg, 20 mg, or 40 mg of omeprazole in the form of enteric-coated granules with the following inactive ingredients: cellulose, disodium hydrogen phosphate, hydroxypropyl cellulose, hydroxypropyl methylcellulose, lactose, mannitol, sodium lauryl sulfate, and other ingredients. The capsule shells have the following inactive ingredients: gelatin NF, FD&C Blue No. 1, FD&C Red No. 40, D&C Red No. 28, titanium dioxide, synthetic black iron oxide, isopropanol, butyl alcohol, FD&C Blue No. 2, D&C Red No. 7 Calcium Lake, and, in addition, the 10-mg and 40-mg capsule shells also contain D&C Yellow No. 10.

Oral Rehydration Salt 45 mEq

Bill of Materials			
Scale (mg/g)	**Item**	**Material Name**	**Qty/kg (g)**
811.90	1	Cerelose Powder	811.90
66.57	2	Sodium Chloride	66.57
31.82	3	Sodium Citrate Dihydrate	31.82
70.14	4	Potassium Citrate Monohydrate/Food Grade	70.14
19.57	5	Povidone (K 29-32)	19.57
—	6	Alcohol	500.00 ml
—	7	Water Purified	50.00 ml

MANUFACTURING DIRECTIONS

1. Mill the dextrose through a 1.2-mm aperture screen or similar on a comminuting mill, medium speed, knives forward.
2. Individually mill the sodium chloride, sodium citrate, and potassium citrate through a 1.2-mm aperture screen on a comminuting mill, medium speed, knives forward.
   Note: Do not mix the milled items until ready to add them to the dextrose.
3. Charge the powders from steps above into a suitable mass mixer and mix for 10 min. Screen the povidone through a 1.2-mm aperture screen and transfer to the mixer. Mix all the powders for 5 min.
4. Mix 500 ml of alcohol with 50 ml of water and slowly add to the mixer while mixing. Continue to mix for 5–10 min. Do not over wet the mass.
5. Granulate the wet mass through a 4.76-mm aperture screen using an oscillating granulator and spread on stainless steel trays.
6. Dry the granules at 45°C for approximately 16 h or until loss on drying is below 0.8%.
7. Turn the granules over after 3–4 h drying.
8. Screen dried granules through an 840-µm aperture screen.
9. Transfer the fine powder to a suitable blender.
10. Pass coarse granules through an 840-µm aperture screen using an oscillating granulator and transfer to the blender. Blend for 5–10 min.
11. Discharge into polyethylene-lined drums.
12. Fill 3.08 g for 100 ml, 7.70 g for 250 ml, and 30.80 g for 1000 ml of reconstituted solution; prorate weights for different volumes.

Orlistat Capsules

Orlistat is a lipase inhibitor for obesity management that acts by inhibiting the absorption of dietary fats. Orlistat is (S)-2-formylamino-4-methyl-pentanoic acid (S)-1-[[(2S, 3S)-3-hexyl-4-oxo-2-oxetanyl] methyl]-dodecyl ester. Orlistat is available for oral administration in dark blue, hard gelatin capsules, with light blue imprinting. Each capsule contains 120 mg of the active ingredient, orlistat. The capsules also contain the inactive ingredients microcrystalline cellulose, sodium starch glycolate, sodium lauryl sulfate, povidone, and talc. Each capsule shell contains gelatin, titanium dioxide, and FD&C Blue No. 1, with printing of pharmaceutical glaze, titanium dioxide, and FD&C Blue No. 1 Aluminum Lake.

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
120.00	1	Orlistat	120.00
93.60	2	Microcrystalline Cellulose	93.60
7.20	3	Sodium Starch Glycolate	7.20
12.00	4	Polyvinylpyrrolidone	12.00
7.20	5	Sodium Lauryl Sulfate	7.20

MANUFACTURING DIRECTIONS

1. Polyvinylpyrrolidone and sodium lauryl sulfate are dissolved in water.
2. Orlistat, microcrystalline cellulose, and sodium starch glycolate are mixed for 10 min and granulated with the solution of Step 1.
3. Granules are dried at or below 30°C and passed through a No. 20 mesh screen.
4. Granules are filled in a size 1 hard gelatin capsule.

Oseltamivir Phosphate Capsules and Oral Suspension

Oseltamivir phosphate is a white crystalline solid with the chemical name (3R,4R,5S)-4-acetylamino-5-amino-3(1-ethylpropoxy)-1-cyclohexene-1-carboxylic acid, ethyl ester, phosphate (1:1). The molecular weight is 312.4 for oseltamivir free base and 410.4 for oseltamivir phosphate salt.

Oseltamivir phosphate is available as a capsule containing 75 mg oseltamivir for oral use, in the form of oseltamivir phosphate, and as a powder for oral suspension, which when constituted with water as directed contains 12 mg/ml oseltamivir. In addition to the active ingredient, each capsule contains pregelatinized starch, talc, povidone K 30, croscarmellose sodium, and sodium stearyl fumarate. The capsule shell contains gelatin, titanium dioxide, yellow iron oxide, black iron oxide, and red iron oxide. Each capsule is printed with blue ink, which includes FD&C Blue No. 2 as the colorant. In addition to the active ingredient, the powder for oral suspension contains xanthan gum, monosodium citrate, sodium benzoate, sorbitol, saccharin sodium, titanium dioxide, and tutti-frutti flavoring.

Oxcarbazepine Oral Suspension

Oxcarbazepine is an antiepileptic drug available as a 300 mg/5 ml (60 mg/ml) oral suspension. Oxcarbazepine is 10,11-dihydro-10-oxo-5*H*-dibenz[b,*f*]azepine-5-carboxamide. The oral suspension contains the following inactive ingredients: ascorbic acid; dispersible cellulose; ethanol; macrogol stearate; methyl parahydroxybenzoate; propylene glycol; propyl parahydroxybenzoate; purified water; sodium saccharin; sorbic acid; sorbitol; yellow-plum-lemon aroma.

Oxycodone Hydrochloride and Acetaminophen Capsules

Each capsule contains oxycodone hydrochloride USP 5 mg and acetaminopohen 500 mg. Inactive ingredients: docusate sodium, gelatin, magnesium stearate, sodium benzoate, sodium metabisulfite, cornstarch, FD&C Blue No. 1, FD&C Red No. 3, FD&C Red No. 40, and titanium dioxide.

Oxytetracycline Hydrochloride Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
250.00	1	Oxytetracycline, USE Oxytetracycline HCl BP 80	275.00
30.00	2	Starch (Cornstarch Dried)	30.00
1.00	3	Colloidal Silicon Dioxide (Aerosil 200)	1.00
3.00	4	Magnesium Stearate	3.00
3.00	5	Talc (Fine Powder)	3.00
1	6	Empty Hard Gelatin Capsule, Size 1	1000

MANUFACTURING DIRECTIONS

Note: The processing area must be under controlled room temperature and humidity. The limits are: RH 50–55%; temperature 22–27°C.

1. Pass Item 1 through a 630-µm sieve, using a sifter. Collect in stainless steel drum.
2. Mix Items 5, 3, and 2 in stainless steel drum. Pass through a 250-µm sieve, using a sifter. Collect in a stainless steel drum.
3. Add 66.67 g of sieved Item 1 (from Step 1) to the drum at Step 2, and mix for 5 min in drum blender.
4. Pass the mix through a 630-µm stainless steel sieve using sifter. Collect in stainless steel drum.
5. Pass Item 4 through a 250-µm sieve using sifter. Collect in stainless steel drum.
6. Add 8.0 g of sieved Item 1 (from Step 1) to the drum at Step 4 and mix for 5 min by rolling.
7. Pass the mix through a 630-µm stainless steel sieve using sifter. Collect in stainless steel drum.
8. Load the sieved powders to the blender. Mix for 5 min.
9. Unload the powder in stainless steel drum.
10. A fill weight of one capsule is 312 mg.

Oxytetracycline Hydrochloride, Sulfamethizole, and Phenazopyridine Hydrochloride Capsules

Each capsule contains: tetracycline hydrochloride equivalent to 250 mg oxytetracycline; sulfamethizole 250 mg; phenazopyridine hydrochloride 50 mg. Inert ingredients in the formulation are: hard gelatin capsules (which may contain FD&C Green No. 3, FD&C Yellow No. 6, D&C Yellow No. 10, and other inert ingredients); magnesium stearate; sodium lauryl sulfate; and starch.

Pancrealipase Capsules

The delayed-release microsphere capsules for delayed release of pancrealipase, which is of porcine pancreatic origin, contain lipase (5000 USP units), protease (18,750 USP units), and amylase 16,600 (USP units) or pancrealipase (10,000 USP units), protease (37,500 USP units), and amylase (33,200 USP units) or contain lipase (20,000 USP units), protease (75,000 USP units), and amylase (66,400 USP units). Inactive ingredients include: dibutyl phthalate, dimethicone, hydroxypropyl methylcellulose phthalate, light mineral oil, and polyethylene glycol. The capsule shells contain gelatin, red iron oxide, titanium dioxide, and yellow iron oxide. The capsule shell contains FD&C Blue No. 2. In addition, the 10,000-unit capsule shell contains black iron oxide and the imprinting ink contains dimethicone, 2-ethoxyethanol, shellac, soya lecithin, and titanium dioxide.

Pancrealipase Capsules Enteric-Coated Microspheres

Pancrealipase capsules are orally administered capsules containing enteric-coated microspheres of porcine pancreatic enzyme concentrate, predominantly pancreatic lipase, amylase, and protease. The inactive ingredients are: povidone, talc, sugar, methacrylic acid copolymer (Type C), triethyl citrate, and simethicone emulsion.

Penicillamine Capsules

Penicillamine is a chelating agent used in the treatment of Wilson's disease. It is also used to reduce cystine excretion in cystinuria and to treat patients with severe, active rheumatoid arthritis unresponsive to conventional therapy. It is 3-mercapto-D-valine. Capsules of penicillamine for oral administration contain either 125 mg or 250 mg of penicillamine. Each capsule contains the following inactive ingredients: D&C Yellow No. 10, gelatin, lactose, magnesium stearate, and titanium dioxide. The 125-mg capsule also contains iron oxide.

Pentosan Polysulfate Sodium Capsules

Pentosan polysulfate sodium is a semi-synthetically produced heparin-like macromolecular carbohydrate derivative, which chemically and structurally resembles glycosaminoglycans. It is a white odorless powder, slightly hygroscopic and soluble in water to 50% at pH 6. It has a molecular weight of 4000 to 6000 Da. It is supplied in white opaque hard gelatin capsules containing 100 mg of pentosan polysulfate sodium, microcrystalline cellulose, and magnesium stearate. It is formulated for oral use.

Pentostatin Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
5.00	1	Pentostatin	5.00
25.00	2	Gelatin	25.00
100.00	3	Lactose	100.00
2.00	4	Iron Oxide Red	2.00

MANUFACTURING DIRECTIONS

1. Pass Items 1–3 through 80 mesh and blend.
2. Add Item 4 and mix for 10 min.
3. Fill 132 mg in a size 1 capsule.

Phenobarbital and Hyoscyamine Sulfate Capsules

Each capsule contains phenobarbital (16.2 mg) and hyoscyamine sulfate (0.1037 mg). The inactive ingredients include: cornstarch, edible ink, D&C Yellow No. 10 and FD&C Green No. 3, or FD&C Blue No. 1 and FD&C Yellow No. 6, FD&C Blue No. 2 Aluminum Lake, gelatin, lactose, sucrose. Capsules may contain FD&C Red No. 40 and Yellow No. 6 aluminum lakes.

Phenoxybenzamine Hydrochloride Capsules

Each capsule, with a red cap and a red body contains phenoxybenzamine hydrochloride (10 mg). Inactive ingredients consist of benzyl alcohol, cetylpyridinium chloride, D&C Red No. 33, FD&C Red No. 3, FD&C Yellow No. 6, gelatin, lactose, sodium lauryl sulfate, and trace amounts of other inactive ingredients.

Phentermine Capsules

Each capsule contains 15 mg or 30 mg of phentermine as the cationic exchange resin complex. Phentermine is (alpha), (alpha)-dimethyl phenethylamine (phenyl-tertiary-butylamine). The inactive ingredients are: D&C Yellow No. 10, dibasic calcium phosphate, FD&C Yellow No. 6, gelatin, iron oxides (15 mg capsules only), lactose, magnesium stearate, and titanium dioxide.

Phentermine Hydrochloride Capsules

Phentermine hydrochloride has the chemical name of (α), (α)-dimethylphenethylamine hydrochloride. It is an anorectic agent for oral administration, is available as a capsule or tablet containing 37.5 mg of phentermine hydrochloride (equivalent to 30 mg of phentermine base). The capsules contain the following inactive ingredients: cornstarch, gelatin, lactose monohydrate, magnesium stearate, titanium dioxide, black iron oxide, FD&C Blue No. 1, FD&C Red No. 40, and D&C Red No. 33.

Phenytoin Sodium Extended-Release Capsules

Phenytoin sodium is an antiepileptic drug. Phenytoin sodium is related to the barbiturates in chemical structure, but has a five-membered ring. Each extended phenytoin sodium capsule contains 30 mg or 100 mg phenytoin sodium. The capsule also contains lactose, confectioner's sugar, talc, and magnesium stearate. The capsule shell and band contain colloidal silicon dioxide, FD&C Red No. 3, gelatin, glyceryl monooleate, and sodium lauryl sulfate. The 30-mg capsule shell and band also contain citric acid, FD&C Blue No. 1, sodium benzoate, and titanium dioxide. The 100-mg capsule shell and band also contain FD&C Yellow No. 6, purified water, and polyethylene glycol 200. Product *in vivo* performance is characterized by a slow and extended rate of absorption with peak blood concentrations expected in 4 to 12 h as contrasted with prompt phenytoin sodium capsules with a rapid rate of absorption with peak blood concentration expected in $1^1/_2$ to 3 h.

Piroxicam and Beta-cyclodextrin Topical Powder

Bill of Materials			
Scale (mg/g)	**Item**	**Material Name**	**Qty/kg (g)**
100.00	1	Piroxicam	100.00
900.00	2	Beta-cyclodextrin	900.00

MANUFACTURING DIRECTIONS

1. Items 1 and 2 are screened through a 60-mesh screen and fed into the grinding chamber of a high-energy vibration mill together. While maintaining the mill at its minimum vibrational frequency, the powders are exposed for 15 min to a flow of steam by opening a connection valve between the chamber and a steam reservoir (mixing and activation stage).
2. After this operation, the true co-grinding stage is continued for 4 h. On termination, the product is discharged, screened through a 60-mesh screen, and homogenized by mixing.

Piroxicam Capsules

Piroxicam is a member of the oxicam group of nonsteroidal anti-inflammatory drugs. Each maroon and blue capsule contains 10 mg of piroxicam; each maroon capsule contains 20 mg of piroxicam for oral administration. The chemical name for piroxicam is 4-hydroxyl-2-methyl-*N*-2-pyridinyl-2 *H*-1, 2-benzothiazine-3-carboxamide 1,1-dioxide. The inactive ingredients in FELDENE capsules include: FD&C Blue No. 1, FD&C Red No. 3, lactose, magnesium stearate, sodium lauryl sulfate, and starch.

1.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
20.00	1	Piroxicam	20.00
233.23	2	Lactose	233.23
48.75	3	Cornstarch	48.75
1.36	4	Magnesium Stearate	1.36
0.15	5	Sodium Lauryl Sulfate	0.15

Note: For 5 and 10 mg strength, adjust with Item 2.

MANUFACTURING DIRECTIONS

1. Charge Items 1–3 in a suitable blender in a low-humidity area.
2. Compress to make slugs, reduce slugs by passing through a No. 20 sieve.
3. Add and blend Items 4 and 5, and blend for 10–15 min.
4. Fill 305 mg in hard gelatin capsules.

2.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
50.00	1	Piroxicam	50.00
124.40	2	Lactose Anhydrous	124.40
50.00	3	Cornstarch	50.00
12.50	4	Sodium Starch Glycolate	12.50
2.50	5	Povidone	2.50
7.50	6	Polysorbate 80	7.50
0.625	7	Colloidal Silicon Dioxide	0.625
6.25	8	Glycine	6.25
1.25	9	Citric Acid	1.25
QS	10	Water Purified	QS

MANUFACTURING DIRECTIONS

1. An aqueous wet granulation process is whereby Item 1, lactose, cornstarch, sodium starch glycolate, colloidal silicon dioxide, and povidone are mixed and subsequently granulated with polysorbate dissolved in purified water.
2. Additional purified water is then added until granules form and no dry powder remains.
3. Glycine and citric acid are dissolved in the additional purified water.
4. Wet granules are dried at 60°C until loss on drying is not more than 2%.
5. The dried granules are milled with the sodium starch glycolate, blended and lubricated with screened magnesium stearate in a twinshell blender.
6. Fill 250 mg in size 2 capsules.

Polyethylene Glycol 3350 Powder for Reconstitution

A white powder. Polyethylene glycol 3350 is a synthetic polyglycol having an average molecular weight of 3350. The actual molecular weight is not less than 90% and not greater than 110% of the nominal value. At below 55°C it is a free-flowing white powder freely soluble in water. It is an osmotic agent for the treatment of constipation. Each dose consists of 17 g of polyethylene glycol 3350.

Polythiazide Capsules

Polythiazide is an orally effective, nonmercurial diuretic, saluretic, and antihypertensive agent. It is designated chemically as 2*H*-1,2,4-benzothiadiazine-7-sulfonamide, 6-chloro-3,4-dihydro-2-methyl-3-[[(2,2,2-tri-fluoro-ethyl)thio]methyl]-,1,1-dioxide. Inert ingredients in the formulations are: hard gelatin capsules (which may contain FD&C Blue No. 1, FD&C Green No. 3, FD&C Red No. 3, and other inert ingredients); magnesium stearate; sodium lauryl sulfate; starch; and sucrose.

Potassium Chloride Extended-Release Capsules

The extended release capsules contain microencapsulated potassium chloride 600 and 750 mg, respectively, of potassium chloride USP equivalent to 8 and 10 mEq of potassium. Dispersibility of potassium chloride (KCl) is accomplished by microencapsulation and a dispersing agent. The resultant flow characteristics of the KCl microcapsules and the controlled release of K + ions by the microcapsular membrane are intended to avoid the possibility that excessive amounts of KCl can be localized at any point on the mucosa of the gastrointestinal tract. Each crystal of KCl is microencapsulated by a patented process with an insoluble polymeric coating which functions as a semi-permeable membrane; it allows for the controlled release of potassium and chloride ions over an 8- to 10-h period. Fluids pass through the membrane and gradually dissolve the potassium chloride within the microcapsules. The resulting potassium chloride solution slowly diffuses outward through the membrane. The inactive ingredients present are edible ink, ethylcellulose, FD&C Blue No. 2 Aluminum Lake, FD&C Yellow No. 6, gelatin, magnesium stearate, sodium lauryl sulfate, and titanium dioxide. The capsules may contain FD&C Red No. 40 and Yellow No. 6 Aluminum Lake.

Potassium Chloride for Oral Solution

Natural fruit-flavored potassium chloride for oral solution, USP is an oral potassium supplement offered in individual packets as a powder for reconstitution. Each packet of powder contains potassium 20 mEq and chloride 20 mEq provided by potassium chloride 1.5 g. It is an electrolyte replenisher. Inactive ingredients: FD&C Yellow No. 6, maltodextrin (contains corn derivative), malic acid, saccharin, silica gel, and natural flavoring.

Potassium Chloride Microencapsulated Sustained-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
600.00	1	Potassium Chloride	600.00
900.00	2	Gelatin	900.00
QS	3	Water Purified	1.5 l
QS	4	Corn Oil	QS
QS	5	Petroleum Ether	QS
QS	6	Isopropyl Alcohol	QS
QS	7	Glutaryldehyde 1%	QS

MANUFACTURING DIRECTIONS

1. Item 2 is added to 1.5 l of Item 3 and the mixture is allowed to stand at 25°C for 1 h while the gelatin hydrates and swells.
2. To this mixture is added Item 1 and the preparation is heated to 60°C while it is stirred at 300 rpm for 30 min to effect dissolution of the gelatin and to assure even suspension of the calcium carbonate. Additional distilled water previously heated to 60°C is then added to bring the total volume to 100°C while the stirring is continued.
3. This preparation is slowly poured into 12 l of a mixture consisting of 20% by volume of corn oil in petroleum ether, which has previously been heated to 60°C while the petroleum ether solution is stirred at 500 rpm. This preparation is then cooled to 5°C with continued stirring, and the stirring is continued at 500 rpm for 1 h after the lower temperature is reached.
4. Isopropanol (6 l) is then added while stirring of the preparation at 5°C is continued. The solid microspheres are then collected by filtration and washed three times with isopropyl alcohol. The capsules are then immersed in 1.5 l of a 1% solution of glutaraldehyde in isopropyl alcohol for 8 h at 5°C, then washed again three times with isopropyl alcohol, filtered, and vacuum dried for 24 h.
5. The microspheres, which average between 200 and 300 μm in diameter, are filled into gelatin capsules for administration as a long-acting antacid product (1.5 g of the microsphere mix, which contains 600 mg of potassium chloride, are filled into each size 00 capsule). This final dosage form delivers a total dose of 600 mg of KCl, but over a sustained time period of 1–4 h and in such a way that the potassium chloride is in the solution state, rather than the more injurious solid state, when it contacts the gastrointestinal mucosa. Total dissolution of the microspheres occurs from 1–5 h after the drug content is depleted.

Potassium Chloride Powder 20 mEq

Bill of Materials			
Scale (g/3g Pack)	**Item**	**Material Name**	**Qty/kg (g)**
1.50	1	Potassium Chloride Powder	500.00
0.40	2	Calcium Cyclamate Granules	130.00
4.00 mg	3	Dye Yellow	1.33
0.16	4	Malic Acid	51.67
0.50	5	Hydrolyzed Cereal Solids	165.00
—	6	Alcohol Anhydrous	90.00
—	7	Water Purified	10.00
15.00	8	Silicon Dioxide Colloidal	15.00
0.25	9	Flavor	81.66
0.20	10	Flavor	65.33

MANUFACTURING DIRECTIONS

1. Pass Items 1–4 and, if necessary, Item 5 through a 686-μm mesh using a comminuting mill with impact forward.
2. Charge the materials from Step 1 and Item 5 in a suitable mixer and mix for 20 min.
3. Mix Items 6 and 7 separately and add to Step 2; mix for 5 min or until satisfactory mass is obtained.
4. Spread wet granules on paper-lined trays and dry at 40–60°C to not more than 1.5% loss on drying.
5. Sift granules through an 840-μm aperture, and grind through a 1.27-mm aperture.
6. Screen the flavors and, if necessary, Item 8 through 20 mesh.
7. Load half the granulation in a blender and add Step 6, followed by remainder granules and blend for 20–30 min.
8. Fill in suitable sachet 3 g.
9.

Prazosin and Polythiazide Capsules

Prazosin hydrochloride, a quinazoline derivative, is the first of the chemical class of antihypertensives. It is the hydrochloride salt of 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furoyl) piperazine. Each 1 mg capsule of contains drug equivalent to 1 mg free base. Inert ingredients in the formulations are: hard gelatin capsules (which may contain FD&C Blue No. 1, FD&C Red No. 3, FD&C Red No. 28, FD&C Red No. 40, and other inert ingredients); magnesium stearate; sodium lauryl sulfate; starch; and sucrose.

Prednisolone Targeted-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
10.00	1	Prednisolone	10.00
100.00	2	Succinic Acid	100.00
30.00	3	Eudragit E100 (5%)	30.00
100.00	4	Hydroxypropyl Methylcellulose Acetate Succinate	100.00
QS	5	Ethanol	QS
QS	6	Purified Water	QS
QS	7	Talc	QS

MANUFACTURING DIRECTIONS

1. Add Items 1 and 2 to a suitable mixer, and blend well. Fill in a size 2 capsule, the core capsule.
2. Spray-coat the core capsule with a 5% by weight solution of Eudragit E100 dissolved in ethanol, in a coating amount of 30 mg per capsule (48% by weight, based on the weight of the used empty hard capsule) as Eudragit E100 to obtain a capsule coated with a low pH-soluble polymer film.
3. The coated capsule is further spray-coated with a coating solution prepared by dissolving Item 4 in a mixture of ethanol and water (5:3 [w/w]) to obtain a 5% by weight Item 4 solution and adding thereto talc in an amount of 2.5% by weight, based on the total weight of the 5% Item 4 solution, in a coating amount of 100 mg per capsule (159% by weight, based on the weight of the used empty hard capsule) as Item 4 by means of an appropriate coater.
4. The formulation described above releases in the lower part of the digestive tract.

Procarbazine Hydrochloride Capsules

Procarbazine hydrochloride, a hydrazine derivative antineoplastic agent, is available as capsules containing the equivalent of 50 mg of procarbazine as the hydrochloride. Each capsule also contains cornstarch, mannitol and talc. Gelatin capsule shells contain parabens (methyl and propyl), potassium sorbate, titanium dioxide, FD&C Yellow No. 6 and D&C Yellow No. 10. Chemically, procarbazine hydrochloride is N-isopropyl-(alpha)-(2-methylhydrazino)-p-toluamide monohydrochloride. It is a white to pale yellow crystalline powder, which is soluble but unstable in water or aqueous solutions. The molecular weight of procarbazine hydrochloride is 257.76.

Prochlorperazine Sustained-Release Capsules

Prochlorperazine is a phenothiazine derivative, present in *Spansule*® sustained release capsules as the maleate. Its chemical name is 2-chloro-10-[3-(4-methyl-1-piperazinyl)propyl]-10 *H* phenothiazine *Z)*-2-butenedioate (1:2). Spansule sustained release capsules — each Compazine *Spansule* is so prepared that an initial dose is released promptly and the remaining medication is released gradually over a prolonged period. Food slows absorption of prochlorperazine and decreases C_{max} by 23% and AUC by 13%. Inactive ingredients consist of ammonio methacrylate co-polymer, D&C Green No. 5, D&C Yellow No. 10, FD&C Blue No. 1, FD&C Blue No. 1 Aluminum Lake, FD&C Red No. 40, FD&C Yellow No. 6, gelatin, hydroxypropyl methylcellulose, propylene glycol, silicon dioxide, simethicone emulsion, sodium lauryl sulfate, sorbic acid, sugar spheres, talc, triethyl citrate, and trace amounts of other inactive ingredients.

Propoxyphene Hydrochloride, Caffeine, and Aspirin Capsules

Propoxyphene Hydrochloride is an odorless, white crystalline powder with a bitter taste. It is freely soluble in water. Chemically, it is (2 *S*,3 *R*)-(+)-4-(dimethylamino)-3-methyl-1,2-diphenyl-2-butanol propionate (ester) hydrochloride. Each capsule contains 65 mg (172.9 µmol) of propoxyphene hydrochloride, 389 mg (2159 µmol) of aspirin, and 32.4 mg (166.8 µmol) of caffeine. It also contains FD&C Red No. 3, FD&C Yellow No. 6, gelatin, glutamic acid hydrochloride, iron oxide, kaolin, silicone, titanium dioxide, and other inactive ingredients.

Propoxyphene Hydrochloride Capsules

Each Pulvule contains 65 mg (172.9 µmol) (No. 365) of propoxyphene hydrochloride. It also contains D&C Red No. 33, FD&C Yellow No. 6, gelatin, magnesium stearate, silicone, starch, titanium dioxide, and other inactive ingredients.

Propranolol Hydrochloride and Hydrochlorothiazide Capsules

Each capsule contains propranolol (80 mg) and hydrochlorothiazide (50 mg); alternately, the capsule may contain 120/50 or 160/50 mg, respectively. It contains the following inactive ingredients: calcium carbonate, ethylcellulose, gelatin capsules, hydroxypropyl methylcellulose, lactose, magnesium stearate, microcrystalline cellulose, sodium lauryl sulfate, sodium starch glycolate, titanium dioxide, and D&C Yellow No. 10. In addition, 80/50-mg and 120/50-mg capsules contain D&C Red No. 33; 120/50-mg and 160/50-mg capsules contain FD&C Blue No. 1 and FD&C Red No. 40.

Propranolol Hydrochloride Long-Acting Capsules

Propranolol hydrochloride is a synthetic beta-adrenergic receptor-blocking agent chemically described as 1-(isopropylamino)-3-(1-naphthyloxy)-2-propanol hydrochloride. It is formulated to provide a sustained release of propranolol hydrochloride. It is is available as 60 mg, 80 mg, 120 mg, and 160 mg capsules. The capsules contain the following inactive ingredients: cellulose, ethylcellulose, gelatin capsules, hydroxypropyl methylcellulose, and titanium dioxide. In addition, Inderal LA® 60 mg, 80 mg, and 120 mg capsules contain D&C Red No. 28 and FD&C Blue No. 1; Inderal LA 160 mg capsules contain FD&C Blue No. 1. These capsules comply with USP Drug Release Test 1.

Propranolol Hydrochloride Multiple Bead Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
160.00	1	Propranolol Hydrochloride [total]	160.00
		Powder Blend	
30.00	1	Propranolol Hydrochloride Powder	30.00
54.00	2	Lactose	54.00
15.00	3	Microcrystalline Cellulose	15.00
1.00	4	Magnesium Stearate	1.00
		pH Sensitive Coated Spheroids	
		Uncoated Spheroids (60% w/w Propranolol Hydrochloride)	3.00 kg
		Methacrylic Acid Copolymer Type B Eudragit S	0.75 kg
		Triacetin	0.112 kg
		Isopropyl Alcohol	1.64 kg
		Methylene Chloride	1.99 kg
		Water	0.50 kg
		Coated Spheroids	
		Uncoated Spheroids (60% w/w Propranolol Hydrochloride)	3.00 kg
		Hydroxypropyl Methylcellulose 2910, 4000 cps, Methocel	0.075 kg
		Methylene Chloride	4.98 kg
		Methanol Anhydrous	2.96
		Eudragit E 30D Aqueous Dispersion	1.00 kg
		Calcium Stearate	0.03 kg
		Simethicone Emulsion	0.0025 kg
		Water Purified	0.50 kg

MANUFACTURING DIRECTIONS

1. The finished dosage form consists of a hard gelatin capsule containing a powder blend of propranolol hydrochloride and two types of spheroids. The formulation particulars are based on 160 mg of propranolol hydrochloride per capsule, although they can be designed to provide other dosage strengths.
2. The propranolol hydrochloride powder blend (or first group of spheroids) provides the loading dose, (e.g., 25 mg of propranolol HCl). The second and third types of spheroids are categorized as:
   a. Propranolol hydrochloride (60 kg) and microcrystalline cellulose (Avicel-PH101; 40 kg) are blended together in a 450-l planetary mixer. Water (50 kg) is added, and the mixer is run for 10 min until a homogeneous plastic mass is obtained. The mass is extruded under pressure through a perforated cylinder to give cylindrical extrudates of nominally 1 mm in diameter. The damp extrudates (in batches of 15 to 20 kg) are placed in a spheronizer in which the rotating disc (diameter 68 cm) rotated at 300 to 400 rpm. The rotation is continued for 10 min, and the resulting spheroids are then dried at 60°C in a fluidized-bed dryer. The dried spheroids are passed over a 1.4-mm screen, and those which passed through are subjected to a 0.7-mm screen. The over- and undersized spheroids are discarded.
   b. pH sensitive coated spheroids are used to provide a second dose (pH 6.5) (e.g., 65 mg propranolol HCl). Uncoated spheroids are placed in a fluidized-bed coater. The Eudragit S solution is applied using a peristaltic pump. The spheroids are dried.
   c. Coated spheroids are used to provide a third dose (4–10 h post-ingestion) (e.g., 70 mg propranolol HCl). The uncoated spheroids are placed in a fluidized-bed coater. Methocel E4MP® solution is sprayed using a peristaltic pump. The spheroids are dried.

3. Process for applying overcoat: Eudragit E 30D suspension containing calcium stearate is sprayed on the Methocel E4MP coated spheroids using a peristaltic pump.
4. The spheroids are dried.
5. Capsules are filled with the powder blend, pH-sensitive coated spheroids, and coated spheroids on an encapsulating machine capable of dual filling powders and spheroids.

Propranolol Hydrochloride Sustained-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
160.00	1	Propranolol Hydrochloride	160.00
128.92	2	Sucrose	128.92
42.97	3	Cornstarch	42.97
22.86	4	Shellac	22.86
35.25	5	Talc	35.25
—	6	Ethyl Alcohol	91.44
—	7	Water Purified	QS

MANUFACTURING DIRECTIONS

I. Neutral Pellets
   A. Weigh and mix in a stainless steel mixer suitable quantities of sucrose and cornstarch in the proportion of 3:1 w/w. Sift through a screen of suitable size to break up possible lumps.
   B. Transfer the mixture to a stainless steel coating pan and adjust rotary speed between 20 and 30 rpm to obtain a good tumbling action.
   C. By means of a suitable spray gun, spray over the powder a quantity of water equal to 15% w/w in very minute drops.
   D. Place the wet pellets over a thermostatic tray dryer and dry at 37°C to complete evaporation of water.
   E. Pass the dried pellets through sieves of suitable screens to ensure removal of dust and selection of cores of desired size.

II. Active Pellets
   A. Dissolve Shellac in Ethyl Alcohol. To 65% of this solution add propranolol hydrochloride. (Reserve the remaining 35% of the solution for the film coating.)
   B. Transfer 171.89 kg of neutral pellets obtained from Step I-E to a stainless steel coating pan and adjust the rotation speed between 20 and 30 rpm so as to obtain good tumbling action.
   C. Spray over the neutral pellets the result of Step II-A.
   D. Keep the pan rotating to allow partial evaporation of the solvent.
   E. Complete evaporation of the solvent by drying the pellets in a thermostat at 35°C for 3 days.

III. Film-Coated Pellets
   A. Transfer the active pellets obtained from Step II-E to a stainless steel coating pan and adjust the rotatory speed so as to obtain a good tumbling action.
   B. Spray the pellets as uniformly as possible with the alcoholic solution of shellac reserved from Step II-A.
   C. Spread the wet pellets with talc to prevent agglutination.
   D. Keep the pan rotating to achieve solidification of the film-coating and partial evaporation of the solvent.
   E. Complete evaporation of the solvent by drying the pellets in a thermostat at 35°C for 3 days.

IV. Blending of Pellets
   A. Transfer the film-coated pellets obtained from Step III-E to a stainless steel pan and add a suitable quantity of neutral pellets obtained from Step III-E to obtain the required dosage.
   B. Add a 0.5% w/w talc to eliminate electrostatic charges and mix for 30–35 min.

V. Assembly
   A. Fill the blended pellets obtained from Step IV-B into capsules of size 1 at the weight of 390 mg.

Propranolol Timed- and Sustained-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
80.00	1	Propranolol	80.00
4.14	2	Polyvinyl Pyrrolidone K-30	4.14
55.85	3	Nonpareil Sugar Beads 25–30 Mesh	55.85
2.80	4	Opadry Clear	2.80
2.33	5	Ethyl Cellulose	2.33
0.23	6	Diethyl Phthalate	0.23
—	7	Water Purified	QS
—	8	Acetone	QS
9.75	9	Ethyl Cellulose	9.75
8.57	10	Hydroxypropyl Methylcellulose Phthalate	8.57
3.10	11	Diethyl Phthalate	3.10

MANUFACTURING DIRECTIONS

1. Prepare a solution of Item 2 in Item 7, and add Item 1 slowly; mix well. This is the drug solution.
2. In a Glatt fluid-bed dryer, charge Item 3 and coat with Step 1 slowly, and then dry to less than 2% moisture.
3. Apply Item 4 coating to dried granules from Step 2 to obtain 2% weight gain.
4. In a separate vessel, prepare a solution of Items 5 and 6 in 98 parts of Item 8 and 2 parts of Item 7. Spray this inner coating on to Step 3.
5. Prepare an acetone:water solution of Items 9–11 and coat on Step 4.
6. Dry and fill in capsules to yield 80, 120, and 160 mg of Item 1. This product provides drug loading of 56% w/w based on core composition corresponding to 45.7% drug based on final time and sustained release beads.

Pseudoephedrine and Guaifenesin Capsules

Each capsule contains: pseudoephedrine hydrochloride 120 mg in a specially prepared base to provide prolonged action and guaifenesin 250 mg designed for immediate release to provide rapid action. Alternate dosing is 60 mg and 300 mg, respectively. The capsules also contain as inactive ingredients: calcium stearate, FD&C Blue No. 1 (for higher strength identification), gelatin, pharmaceutical glaze, starch, sucrose, talc, and titanium dioxide.

Pseudoephedrine Hydrochloride Capsules

Bill of Materials			
Scale (mg/Capsule)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
24.00	1	Pseudoephedrine Hydrochloride	24.00
15.00	2	Hydroxyethylcellulose NF	15.00
60.00	3	Lactose Anhydrous	60.00
1.00	4	Magnesium Stearate	1.00

MANUFACTURING DIRECTIONS

Blend all the ingredients in a twinshell blender for 10 min. Fill size 0 capsules with fill weight of 500 mg, using tamping force of 200 N.

Ranitidine Effervescent Granules

Ranitidine hydrochloride (HCl) is a histamine H2-receptor antagonist. Chemically, it is N[2-[[[5-[(dimethylamino)methyl]-2-furanyl]methyl]thio]ethyl]-N′-methyl-2-nitro-1,1-ethenediamine, HCl. Granules for oral administration are effervescent formulations of ranitidine; these must be dissolved in water before use. Each packet contains 168 mg of ranitidine HCl equivalent to 150 mg of ranitidine and the following inactive ingredients: aspartame, monosodium citrate anhydrous, povidone, and sodium bicarbonate.

Ribavirin Capsules

Ribavirin is a nucleoside analog with antiviral activity. The chemical name of ribavirin is 1-(beta)-D-ribofuranosyl-1 *H*-1,2,4-triazole-3-carboxamide. Capsules consist of a white powder in a white opaque gelatin capsule. Each capsule contains 200 mg of ribavirin and the following inactive ingredients: microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, and magnesium stearate. The capsule shell consists of gelatin and titanium dioxide. The capsule is printed with edible blue pharmaceutical ink, which is made of shellac, anhydrous ethyl alcohol, isopropyl alcohol, n-butyl alcohol, propylene glycol, ammonium hydroxide, and FD&C Blue No. 2 aluminum lake.

Rifabutin Capsules

The antimycobacterial agent rifabutin is a semisynthetic ansamycin antibiotic derived from rifamycin S. The capsules contain 150 mg of rifabutin, USP, per capsule, along with the following inactive ingredients: microcrystalline cellulose, magnesium stearate, red iron oxide, silica gel, sodium lauryl sulfate, titanium dioxide, and edible white ink.

Rifampicin Capsules

Rifampicin (rifampin) capsules contain 150 mg or 300 mg of rifampin per capsule. The 150-mg and 300-mg capsules also contain, as inactive ingredients: cornstarch, D&C Red No. 28, FD&C Blue No. 1, FD&C Red No. 40, gelatin, magnesium stearate, and titanium dioxide. Rifampin is a semisynthetic antibiotic derivative of rifamycin SV. Rifampin is a red-brown crystalline powder very slightly soluble in water at neutral pH, freely soluble in chloroform, soluble in ethyl acetate and in methanol.

Rifampin and Isoniazid Capsules

This is a combination capsule containing 300 mg of rifampin and 150 mg of isoniazid. The capsules also contain as inactive ingredients: colloidal silicon dioxide, FD&C Blue No. 1, FD&C Red No. 40, gelatin, magnesium stearate, sodium starch glycolate, and titanium dioxide. Rifampin is a semisynthetic antibiotic derivative of rifamycin B. The chemical name for rifampin is 3-(4-methyl-1-piperazinyliminomethyl) rifamycin SV. Isoniazid is the hydrazide of isonicotinic acid. It exists as colorless or white crystals or as a white crystalline powder that is water soluble, odorless, and slowly affected by exposure to air and light.

Rivastigmine Tartrate Capsules

Rivastigmine tartrate is a reversible cholinesterase inhibitor and is known chemically as (S)-N-Ethyl-N-methyl-3-[1-(dimethylamino)ethyl]-phenyl carbamate hydrogen-(2*R*,3*R*)-tartrate. Rivastigmine tartrate is commonly referred to in the pharmacological literature as SDZ ENA 713 or ENA 713. It is supplied as capsules containing rivastigmine tartrate, equivalent to 1.5, 3, 4.5, and 6 mg of rivastigmine base for oral administration. Inactive ingredients are hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, and silicon dioxide. Each hard gelatin capsule contains gelatin, titanium dioxide, and red and/or yellow iron oxides.

Salmeterol Xinafolate Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
2.00	1	Salmeterol Xinafolate	2.00
97.00	2	Starch 1500 DC	97.00
1.00	3	Magnesium Stearate	1.00

MANUFACTURING DIRECTIONS

Blend and fill 100 mg in each capsule.

Salmeterol Xinafolate Inhalation Powder

Salmeterol xinafolate inhalation powder contains salmeterol xinafolate as the racemic form of the 1-hydroxy-2-naphthoic acid salt of salmeterol. The active component of the formulation is salmeterol base, a highly selective beta 2-adrenergic bronchodilator. The chemical name of salmeterol xinafolate is 4-hydroxy-(alpha) 1-[[[6-(4-phenylbutoxy) hexyl]amino]methyl]-1,3-benzenedimethanol, 1-hydroxy-2-naphthalenecarboxylate. It is a specially designed plastic device containing a double-foil blister strip of a powder formulation of salmeterol xinafolate intended for oral inhalation only. Each blister on the double-foil strip within the device contains 50 mcg of salmeterol administered as the salmeterol xinafolate salt in 12.5 mg of formulation containing lactose. When a blister containing medication is opened by activating the device, the medication is dispersed into the air stream created when the patient inhales through the mouthpiece.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
0.05	1	Salmeterol Xinafolate Micronized	0.05
12.50	2	Lactose Anhydrous	12.50

Saquinavir Mesylate Capsules

Saquinavir mesylate is an inhibitor of the human immunodeficiency virus (HIV) protease. The chemical name for saquinavir mesylate is N-tert-butyl-decahydro-2-[2(R)-hydroxy-4-phenyl-3(S)-[[N-(2-quinolylcarbonyl)-L-asparaginyl]amino]butyl]-(4aS,8aS)-isoquinoline-3(S)-carboxamide methanesulfonate. It is available as light brown and green, opaque hard gelatin capsules for oral administration in a 200-mg strength (as saquinavir free base). Each capsule also contains the inactive ingredients: lactose, microcrystalline cellulose, povidone K30, sodium starch glycolate, talc, and magnesium stearate. Each capsule shell contains gelatin and water with the following dye systems: red iron oxide, yellow iron oxide, black iron oxide, FD&C Blue No. 2, and titanium dioxide. Another formulation contains inactives. Each capsule also contains the inactive ingredients: medium chain mono- and diglycerides, povidone, and dl-alpha tocopherol. Each capsule shell contains gelatin and glycerol 85% with the following colorants: red iron oxide, yellow iron oxide, and titanium dioxide.

Selegiline Hydrochloride

Selegiline hydrochloride is a levorotatory acetylenic derivative of phenethylamine. It is commonly referred to in the clinical and pharmacological literature as l-deprenyl. The chemical name is: (R)-(-)-*N,2*-dimethyl-*N*-*2*-propynylphenethylamine hydrochloride. Each aqua blue capsule contains 5 mg of selegiline hydrochloride. The inactive ingredients are: citric acid, lactose, magnesium stearate, and microcrystalline cellulose.

Sevelamer Hydrochloride Capsules

Sevelamer hydrochloride is a polymeric phosphate binder intended for oral administration. Sevelamer hydrochloride is poly(allylamine hydrochloride) crosslinked with epichlorohydrin in which 40% of the amines are protonated. It is known chemically as poly(allylamine-co-N,N′-diallyl-1,3-diamino-2-hydroxypropane) hydrochloride. Sevelamer hydrochloride is hydrophilic, but insoluble in water. Each hard gelatin capsule of Renagel® contains 403 mg of sevelamer hydrochloride on an anhydrous basis. The inactive ingredients are colloidal silicon dioxide and stearic acid. The capsule and imprint contain titanium dioxide and indigo carmine ink.

Sibutramine Hydrochloride Capsules

Sibutramine hydrochloride monohydrate is an orally administered agent for the treatment of obesity. Chemically, the active ingredient is a racemic mixture of the (+) and (–) enantiomers of cyclobutanemethanamine, 1-(4-chlorophenyl)-*N,N*-dimethyl-(alpha)-(2-methylpropyl)-, hydrochloride, monohydrate. Each capsule contains 5 mg, 10 mg, or 15 mg of sibutramine hydrochloride monohydrate. It also contains as inactive ingredients: lactose monohydrate, NF; microcrystalline cellulose, NF; colloidal silicon dioxide, NF; and magnesium stearate, NF in a hard-gelatin capsule (which contains titanium dioxide, USP; gelatin; FD&C Blue No. 2 [5- and 10-mg capsules only]; D&C Yellow No. 10 [5- and 15-mg capsules only], and other inactive ingredients).

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
5.00	1	Sibutramine Hydrochloride	5.00
78.50	2	Lactose Anhydrous	78.50
5.00	3	Polyvinylpyrrolidone	5.00
15.00	4	Cornstarch	15.00
1.50	5	Magnesium Stearate	1.50
QS	6	Alcohol	QS

MANUFACTURING DIRECTIONS

1. Mix Items 1, 2, and 4 and granulate with alcoholic solution of Item 3.
2. Dry, size, and blend with Item 5.
3. Fill 105 mg; adjust for higher dose with Item 2.

Stavudine Capsules

Stavudine (d4T), a synthetic thymidine nucleoside analog, is active against HIV. The chemical name for stavudine is 2′,3′-didehydro-3′-deoxythymidine. The stavudine capsules are supplied for oral administration in strengths of 15, 20, 30, and 40 mg of stavudine. Each capsule also contains inactive ingredients: microcrystalline cellulose, sodium starch glycolate, lactose, and magnesium stearate. The hard gelatin shell consists of gelatin, silicon dioxide, sodium lauryl sulfate, titanium dioxide, and iron oxides.

Succimer Capsules

Succimer is an orally active, heavy metal chelating agent. The chemical name for succimer is *meso* 2,3-dimercaptosuccinic acid (DMSA). Each opaque white capsule for oral administration contains beads coated with 100 mg of succimer and is imprinted in black with CHEMET 100®. The inactive ingredients in medicated beads are: povidone, sodium starch glycolate, starch, and sucrose. The inactive ingredients in the capsule are: gelatin, iron oxide, titanium dioxide, and other ingredients.

Sucralafate Granules

Bill of Materials			
Scale (mg/Sachet) (2 g)	**Item**	**Material Name**	**Qty/2 kg (g)**
1000.00	1	Sucralafate	1000.00
100.00	2	Cornstarch	100.00
240.00	3	Povidone	240.00
QS	4	Lactose, QS to 2000	QS
—	5	Alcohol	QS

MANUFACTURING DIRECTIONS

1. Charge Items 1 and 2 in a fluid-bed granulator (e.g., Glatt) and mix for 5 min at inlet temperature of 30°C.
2. Dissolve Item 3 in a separate container in Item 5 and spray into Step 1 to granulate.
3. Dry granules at 50°C until the temperature reaches 30°C.
4. Sieve through No. 18.
5. Fill 1.9–2.1 g per sachet.

Tacrine Hydrochloride Capsules

Tacrine hydrochloride is a reversible cholinesterase inhibitor, known chemically as 1,2,3,4-tetrahydro-9-acridinamine monohydrochloride monohydrate. Each capsule contains tacrine as the hydrochloride. Inactive ingredients are hydrous lactose, magnesium stearate, and microcrystalline cellulose. The hard gelatin capsules contain: gelatin, silicon dioxide, sodium lauryl sulfate, and the following dyes: 10 mg: D&C Yellow No. 10, FD&C Green No. 3, titanium dioxide; 20 mg: D&C Yellow No. 10, FD&C Blue No. 1, titanium dioxide; 30 mg: D&C Yellow No. 10, FD&C Blue No. 1, FD&C Red No. 40, titanium dioxide; 40 mg: D&C Yellow No. 10, FD&C Blue No. 1, FD&C Red No. 40, D&C Red No. 28, and titanium dioxide. Each 10-, 20-, 30-, and 40-mg capsule for oral administration contains 12.75, 25.50, 38.25, and 51.00 mg of tacrine hydrochloride, respectively.

Tacrolimus Capsules

Tacrolimus is available for oral administration as capsules (tacrolimus capsules) containing the equivalent of 0.5 mg, 1 mg, or 5 mg of anhydrous tacrolimus. Inactive ingredients include lactose, hydroxypropyl methylcellulose, croscarmellose sodium, and magnesium stearate. The 0.5-mg capsule shell contains gelatin, titanium dioxide, and ferric oxide, the 1-mg capsule shell contains gelatin and titanium dioxide, and the 5-mg capsule shell contains gelatin, titanium dioxide, and ferric oxide. Tacrolimus is a macrolide immunosuppressant produced by *Streptomyces tsukubaensis.*

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
1.00	1	Tacrolimus	1.00
1.00	2	Hydroxypropyl Methylcellulose 2910	1.00
QS	3	Ethanol	QS
58.00	4	Lactose	58.00

MANUFACTURING DIRECTIONS

1. Item 1 is mixed with Items 2 and 3. The mixture is kneaded and granulated to pass through sieves to collect particle size 180–250 μm; the other particle size is regranulated.
2. Dry granulation in Step 1 is dried at room temperature.
3. In a suitable blending vessel, add Item 4 and gradually add the Step 2 granulation. Mix for 10 min and fill in size 0 capsules.

Talc, Crospovidone, and Starch Topical Powder

Bill of Materials			
Scale (mg/g)	**Item**	**Material Name**	**Qty/kg (g)**
100.00	1	Croscarmellose Sodium (Crospovidone)	100.00
800.00	2	Cornstarch	800.00
100.00	3	Talc	100.00

MANUFACTURING DIRECTIONS

Mix and fill in bottles.

Tamsulosin Hydrochloride Capsules

Tamsulosin hydrochloride is an antagonist of alpha 1A adrenoceptors in the prostate. Tamsulosin HCl is (-)-(*R*)-5-[2-[[2-(0-ethoxyphenoxy)ethyl]amino]propyl]-2-methoxybenzenesulfonamide, monohydrochloride. Each capsule for oral administration contains tamsulosin HCl 0.4 mg, and the following inactive ingredients: methacrylic acid copolymer, microcrystalline cellulose, triacetin, polysorbate 80, sodium lauryl sulfate, calcium stearate, talc, FD&C Blue No. 2, titanium dioxide, ferric oxide, gelatin, and trace amounts of shellac, industrial methylated spirit 74 OP, *n*-butyl alcohol, isopropyl alcohol, propylene glycol, dimethylpolysiloxane, and black iron oxide (E172).

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
0.40	1	Tamsulosin Hydrochloride	0.40
35.60	2	Crystalline Cellulose	35.60
13.32	3	Eudragit L30D-55	13.32
4.00	4	Magnesium Stearate	4.00

MANUFACTURING DIRECTIONS

1. After sufficiently mixing Item 1 crystalline cellulose, and of magnesium stearate, a mixture of Eudragit L30D-55 and 40 ml of water was added to the aforementioned mixture, and the resultant mixture was kneaded and granulated by a centrifugal fluidized-bed granulator.
2. The granules obtained were spheres having particle sizes of 0.1 to 1.5 mm, mainly 0.2 to 1.0 mm.

Temazepam Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
7.50	1	Temazepam Micronized	7.50
7.50	2	Lactose Anhydrous	7.50
232.50	3	Lactose Anhydrous	232.50
2.50	4	Magnesium Stearate	2.50

MANUFACTURING DIRECTIONS

1. Item 1 is processed as follows: White crystalline temazepam having a purity of not less than 98% is fed into an Alpine 160 UPZ mill with a stainless steel pin at a rate of about 40 kg per hour using a mill speed of about 11,000 rpm to obtain temazepam particles having a specific surface area of 0.65 to 1.1 m^2/g area and 95% of the particles having a particle size diameter of less than 65 µm. The surface area measurement is made with the Quantector Gas Flow System and Quantasorb Surface Area Analyser at the temperature of liquid nitrogen (−196°C) using krypton as the absorbant and helium as the carrier gas. The particle size diameter is determined with the Malverne Particle Sizer at an obscuration value of 0.2 to 0.25 using a 0.1% Tween 80 solution in water saturated with temazepam in which 1 to 2 g of temazepam sample to be tested has been dispersed. After the feed rate and mill speed of the Alpine mill have been set, they are monitored at regular intervals to maintain the required particle size and surface area.
2. To prepare hard gelatin capsules containing 7.5 mg of the temazepam processed as in Step 1, charge Items 1 and 2 in a mill and pass through an 18-mesh screen.
3. Pass Item 3 through 18-mesh screen and add to Step 2.
4. Pass Item 4 through 18-mesh screen and add to Step 3 in a PK Mixer® without an intensity bar.
5. Mix for 30 min using tumbling action only.
6. The capsule mix is encapsulated in number 3 Lock hard gelatin capsules. Each capsule contains 250 mg of capsule mix and 7.5 mg of temazepam.

Temozolomide Capsules

The chemical name of temozolomide is 3,4-dihydro-3-methyl-4-oxoimidazo[5,1-d]-tetrazine-8-carboxamide. Each capsule contains either 5 mg, 20 mg, 100 mg, or 250 mg of temozolomide. The inactive ingredients for TEMODAR® Capsules are lactose anhydrous, colloidal silicon dioxide, sodium starch glycolate, tartaric acid, and stearic acid. The gelatin capsule shells contain titanium dioxide. The capsules are imprinted with pharmaceutical ink.

Terazosin Hydrochloride Capsules

Terazosin hydrochloride, an alpha-1-selective adrenoceptor blocking agent, is a quinazoline derivative represented by the following chemical name and structural formula: (RS)-piperazine,1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-[(tetra-hydro-2-furanyl)carbonyl]-,monohydrochloride, dihydrate. Terazosin hydrochloride capsules for oral ingestion are supplied in four dosage strengths containing terazosin hydrochloride equivalent to 1 mg, 2 mg, 5 mg, or 10 mg of terazosin. The inactive ingredients in the 1-mg capsules are: gelatin, glycerin, iron oxide, methylparaben, mineral oil, polyethylene glycol, povidone, propylparaben, titanium dioxide, and vanillin; 2-mg capsules: D&C Yellow No. 10, gelatin, glycerin, methylparaben, mineral oil, polyethylene glycol, povidone, propylparaben, titanium dioxide, and vanillin; 5-mg capsules: D&C Red No. 28, FD&C Red No. 40, gelatin, glycerin, methylparaben, mineral oil, polyethylene glycol, povidone, propylparaben, titanium dioxide, and vanillin; 10-mg capsules: FD&C Blue No. 1, gelatin, glycerin, methylparaben, mineral oil, polyethylene glycol, povidone, propylparaben, titanium dioxide, and vanillin.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
5.000	1	Terazosin Hydrochloride Anhydrous	5.471
174.529	2	Lactose Monohydrate	174.529
28.000	3	Microcrystalline Cellulose	28.000
14.000	4	Crospovidone	14.000
3.000	5	Magnesium Stearate	3.000

MANUFACTURING DIRECTIONS

1. Add and blend all Items 1–5 in a suitable blender.
2. Fill using size 3 capsules; fill weight of 225.00 mg.

Tetracycline Hydrochloride Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
250.00	1	Tetracycline, USE Tetracycline	275.00
46.00	2	Lactose Monohydrate (Dense)	46.00
2.00	3	Colloidal Silicon Dioxide (Aerosil 200)	2.00
2.00	4	Magnesium Stearate	2.00
1	5	Empty Hard Gelatin Capsule, Size 1	1000

MANUFACTURING DIRECTIONS

1. Check the temperature and relative humidity of the room before start of processing. Limits: RH 50–55%; temperature: 22–27°C.
2. Pass the Items 1, 2, and 3 through a 630-µm sieve, using a sifter. Collect in stainless steel drum.
3. Pass Item 4 through a 250-µm sieve, using a sifter. Collect in polythene bag. Load the sieved powder to the drum (Step 1) and mix for 5 min using drum mixer.
4. Load the empty capsule shells (size 1) in the hopper.
5. Run the machine and check the locking of shells.
6. Fill weight of one capsule = 325 mg + average weight of one empty shell.

Thalidomide Capsules

Thalidomide, α-(*N*-phthalimido) glutarimide, is an immunomodulatory agent. Thalidomide capsules are available in 50-mg capsules for oral administration. Active ingredient: thalidomide. Inactive ingredients: anhydrous lactose, microcrystalline cellulose, polyvinylpyrrolidone, stearic acid, colloidal anhydrous silica, and gelatin.

Theophylline Sustained-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
150.00	1	Theophylline Anhydrous (B.F. Goodrich)	150.00
26.60	2	Carbopol 934P (GAF Corporation)	26.60
172.10	3	PVP C-15	172.10
3.50	4	Talc	3.50
1.80	5	Zinc Stearate	1.80

MANUFACTURING DIRECTIONS

1. The Carbopol 934P, PVP C-15 (mean molecular weight of about 8000, talc, and zinc stearate are combined in a mixer and are mixed.
2. Theophylline anhydrous is added to this mixture and mixed well to achieve a uniform mixture.
3. The resulting particulate mixture, 354 mg, is filled into size 1 hard gelatin capsule shells.

Thiothixene Capsules

Thiothixene is a thioxanthene derivative. Specifically, it is the *cis* isomer of *N*,*N*-dimethyl-9-[3-(4-methyl-1-piperazinyl)-propylidene] thioxanthene-2-sulfonamide. Each capsule contains 1 mg, 2 mg, 5 mg, or 10 mg of thiothixene and the following inactive ingredients: colloidal silicon dioxide, croscarmellose sodium (Type A), gelatin, magnesium stearate, microcrystalline cellulose, powdered cellulose, pregelatinized starch, sodium lauryl sulfate, titanium dioxide, and other inactive ingredients. The following coloring agents are employed: 1 mg — FD&C Blue No. 1, D&C Red No. 28, FD&C Red No. 40, FD&C Yellow No. 6; 2 mg — FD&C Blue No. 1, FD&C Red No. 40, FD&C Yellow No. 6, D&C Yellow No. 10; 5 mg — FD&C Blue No. 1, FD&C Red No. 40, FD&C Yellow No. 6; 10 mg — FD&C Blue No. 1, FD&C Red No. 40, FD&C Yellow No. 6.

Tibolone Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
0.30	1	Tibolone (Org GD 14)	0.30
1.95	2	Hydroxypropyl Cellulose	1.95
32.50	3	Cornstarch	32.50
0.32	4	Magnesium Stearate	0.32
QS	5	Lactose, QS to	130.00
QS	6	Water Purified	QS

MANUFACTURING DIRECTIONS

1. Charge in a mixer Items 3 and 5 and mix well.
2. Prepare a suspension of Items 1 and 2 in Item 6 and mix thoroughly; add to Step 1 and granulate in a granulator by mixing for 2–3 min.
3. Dry the sieved wet material for 4 h in a vacuum dryer at 40°C.
4. Screen the dried granules through a 710-μm sieve in the drum.
5. Load the empty capsule shells (size 1) in the hopper.
6. Run the machine and check the locking of shells.
7. Fill 130 mg in suitable capsules.

Tiotropium Inhalation Powder

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
21.70	1	Tiotropium Bromide Micronized	21.70
270.00	2	Endothelin Antagonist 2	270.00
4708.30	3	Lactose	4708.30

MANUFACTURING DIRECTIONS

1. Item 1 should first be prepared in an inhalable powder form by the following method:
   a. 15.0 kg of tiotropium bromide are placed in 25.7 kg of water in a suitable reaction vessel.
   b. The mixture is heated to 80–90°C and stirred at constant temperature until a clear solution is formed.
   c. Activated charcoal (0.8 kg) moistened with water is suspended in 4.4 kg of water. This mixture is added to the solution containing the tiotropium bromide and the resulting mixture is rinsed with 4.3 kg of water.
   d. The mixture thus obtained is stirred for at least 15 min at 80–90°C. Then, it is filtered through a heated filter into an apparatus preheated to an external temperature of 70°C.
   e. The filter is rinsed with 8.6 kg of water. The contents of the apparatus are cooled at 3–5°C for every 20 min to a temperature of 20–25°C.
   f. The apparatus is cooled further to 10–15°C using cold water and crystallization is completed by stirring for at least another hour.
   g. The crystals are isolated using a suction filter dryer. The crystals are washed with cold water (10–15°C) and cold acetone (10–15°C).
   h. The crystals obtained are dried at 25°C in a nitrogen current over a period of 2 h. Yield: 13.4 μg of tiotropium bromide monohydrate (86% of theory).
2. Add and mix all items and mix well.
3. Fill 5.00 g per unit dose.

Tolmetin Sodium Capsules

Capsules for oral administration contain tolmetin sodium as the dihydrate in an amount equivalent to 400 mg of tolmetin. Each capsule contains 36 mg (1.568 mEq) of sodium and the following inactive ingredients: gelatin, magnesium stearate, cornstarch, talc, FD&C Red No. 3, FD&C Yellow No. 6, and titanium dioxide.

Tolterodine Capsules

The capsules contain tolterodine tartrate, a muscarinic receptor antagonist. The chemical name of tolterodine tartrate is (R)-*N*,*N*-diisopropyl-3-(2-hydroxy-5-methylphenyl)-3-phenylpropanamine L-hydrogen tartrate. Capsules contain 2 mg or 4 mg of tolterodine tartrate. The inactive ingredients are: sucrose, starch, hydroxypropyl methylcellulose, ethylcellulose, medium chain triglycerides, oleic acid, gelatin, and FD&C Blue No. 2. The 2-mg capsules also contain yellow iron oxide. Both capsule strengths are imprinted with a pharmaceutical grade printing ink that contains shellac, titanium dioxide, propylene glycol, and simethicone.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
2.00	1	Tolterodine	2.00
186.00	2	Lactose Anhydrous	186.00
20.00	3	Cornstarch	20.00
15.00	4	Talc	15.00
2.00	5	Magnesium Stearate	2.00

Note: For 1-mg strength, adjust with Item 2.

MANUFACTURING DIRECTIONS

1. Item 1 is accordingly mixed with Items 2 and 3 and then milled.
2. The resulting mixture is then mixed with ingredients 4 and 5 and then filled into capsules of appropriate size.

Topiramate Capsules

Topiramate is a sulfamate-substituted monosaccharide that is intended for use as an antiepileptic drug. Topiramate capsules, Sprinkle capsules are available as 15 mg and 25 mg sprinkle capsules for oral administration as whole capsules or opened and sprinkled onto soft food. Topiramate is a white crystalline powder with a bitter taste. Topiramate is most soluble in alkaline solutions containing sodium hydroxide or sodium phosphate and having a pH of 9 to 10. It is freely soluble in acetone, chloroform, dimethylsulfoxide, and ethanol. The solubility in water is 9.8 mg/ml. Its saturated solution has a pH of 6.3. Topiramate is designated chemically as 2,3:4,5-Di-*O*-isopropylidene-(beta)-D-fructopyranose sulfamate. Sprinkle capsules contain topiramate coated beads in a hard gelatin capsule. The inactive ingredients are: sugar spheres (sucrose and starch), povidone, cellulose acetate, gelatin, silicon dioxide, sodium lauryl sulfate, titanium dioxide, and black pharmaceutical ink.

Tretinoin Capsules

Tretinoin is a retinoid that induces maturation of acute promyelocytic leukemia (APL) cells in culture. It is available in a 10-mg soft gelatin capsule for oral administration. Each capsule also contains beeswax, butylated hydroxyanisole, edetate disodium, hydrogenated soybean oil flakes, hydrogenated vegetable oils, and soybean oil. The gelatin capsule shell contains glycerin, yellow iron oxide, red iron oxide, titanium dioxide, methylparaben, and propylparaben.

Triamterene and Hydrochlorothiazide Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
23.01	1	Triamterene	23.01
15.34	2	Hydrochlorothiazide	15.34
2.50	3	Glycine	2.50
7.50	4	Polysorbate 80	7.50
QS	5	Water Purified	QS
QS	6	Isopropyl Alcohol	QS
52.15	7	Lactic Acid	52.15

MANUFACTURING DIRECTIONS

1. Add and dissolve Item 3 in a suitable quantity of Item 5.
2. Add Items 1 and 2, and prepare a good wet mass.
3. Separately dissolve Item 4 in Item 6, and add to Step 2 until granules are formed.
4. Dry granules in vacuum and mill.
5. Fill in size 4 capsules.

Triamterene Capsules

Triamterene is a potassium-sparing diuretic. Triamterene is 2,4,7-triamino-6-phenyl-pteridine. Each capsule for oral use, with an opaque red cap and body, contains triamterene, 50 or 100 mg. The inactive ingredients consist of benzyl alcohol, cetylpyridinium chloride, D&C Red No. 33, FD&C Yellow No. 6, gelatin, lactose, magnesium stearate, povidone, sodium lauryl sulfate, titanium dioxide, and trace amounts of other inactive ingredients.

Triclosan and Zinc Undecylenate Powder

Bill of Materials			
Scale (mg/g)	**Item**	**Material Name**	**Qty/1000 Tabs (g)**
3.0	1	Triclosan-Irgasan DP300	3.0
2.0	2	Zinc Undecylenate	2.0
0.2	3	Menthol	0.2
926.8	4	Talc	926.8
30.0	5	Magnesium Stearate	30.0
30.0	6	Cornstarch	30.0
8.0	7	Perfume	8.0

MANUFACTURING DIRECTIONS

1. Pass the following ingredients through a 250-μm aperture screen or similar screen: Triclosan-Irgasan DP300, zinc undecylenate, magnesium stearate, cornstarch, menthol, and approximately 10% of the total amount of talc.
2. Charge materials from first step into a suitable mixer. Mix until uniform.
3. Discharge powder from second step into another suitable mixer. Add and disperse perfume. Mix until uniform. Pass mixture from step above through a 250-μm aperture screen or similar screen. Charge mixture from Step 2 into a V-mixer or a similar mixer, and add balance of talc powder.
4. Mix for 30 min or until homogeneous.

Trientine Hydrochloride Capsules

Trientine hydrochloride is *N,N′*-bis (2-aminoethyl)-1,2-ethanediamine dihydrochloride. Trientine hydrochloride is a chelating compound for removal of excess copper from the body. It is available as 250-mg capsules for oral administration. It contains gelatin, iron oxides, stearic acid, and titanium dioxide as inactive ingredients.

Trimethoprim and Sulfamethoxazole Oral Suspension

Trimethoprim and sulfamethoxazole is a synthetic antibacterial combination product available in DS (double strength) pediatric suspension for oral administration. Each teaspoonful (5 ml) of the pediatric suspension contains 40 mg trimethoprim and 200 mg sulfamethoxazole in a vehicle containing 0.3% alcohol, edetate disodium, glycerin, microcrystalline cellulose, parabens (methyl and propyl), polysorbate 80, saccharin sodium, simethicone, sorbitol, sucrose, FD&C Yellow No. 6, FD&C Red No. 40, flavors, and water.

Trimipramine Maleate Capsules

Trimipramine maleate is 5-(3-dimethylamino-2-methylpropyl)-10,11-dihydro-5H-dibenz(b,f) azepine acid maleate (racemic form). Each capsule contains trimipramine maleate equivalent to 25 mg, 50 mg, or 100 mg of trimipramine as the base. The inactive ingredients present are FD&C Blue 1, gelatin, lactose, magnesium stearate, and titanium dioxide. The 25 mg dosage strength also contains D&C Yellow No. 10 and FD&C Yellow No. 6; the 50 mg dosage strength also contains D&C Red No. 28, FD&C Red No. 40, and FD&C Yellow No. 6.

Troleandomycin Capsules

Troleandomycin is a synthetically derived acetylated ester of oleandomycin, an antibiotic elaborated by a species of *Streptomyces antibioticus.* It is a white crystalline compound, insoluble in water, but readily soluble and stable in the presence of gastric juice. Inert ingredients in the formulation are: hard gelatin capsules (which may contain inert ingredients); lactose; magnesium stearate; sodium lauryl sulfate; and starch.

Typhoid Vaccine Live Oral Capsules

Typhoid vaccine live oral Ty21a is a live attenuated vaccine for oral administration only. The vaccine contains the attenuated strain *Salmonella typhi* Ty21a (1,2). The vaccine is manufactured by the Swiss Serum and Vaccine Institute. The vaccine strain is grown in fermenters under controlled conditions in medium containing a digest of yeast extract, an acid digest of casein, dextrose, and galactose. The bacteria are collected by centrifugation, mixed with a stabilizer containing sucrose, ascorbic and amino acids, and lyophilized. The lyophilized bacteria are mixed with lactose and magnesium stearate and filled into gelatin capsules, which are coated with an organic solution to render them resistant to dissolution in stomach acid. The enteric-coated, salmon/white capsules are then packaged in 4-capsule blisters for distribution. The contents of each enteric-coated capsule are:

Viable *S. typhi* Ty21a	2–6 H 10^9 colony-forming units[a]
Nonviable *S. typhi* Ty21a	5–50 H 10^9 bacterial cells
Sucrose	26–130 mg
Ascorbic acid	1–5 mg
Amino acid mixture	1.4–7 mg
Lactose	100–180 mg
Magnesium stearate	3.6–4.4 mg

[a] Vaccine potency (viable cell counts per capsule) is determined by inoculation of agar plates with appropriate dilutions of the vaccine suspended in physiological saline.

Valsartan and Hydrochlorothiazide Capsules

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
80.00	1	Valsartan	80.00
12.50	2	Hydrochlorothiazide	12.50
1.50	3	Colloidal Anhydrous Silica Aerosil	1.50
31.50	4	Microcrystalline Cellulose Avicel	31.50
20.00	5	Polyvinylpyrrolidone Crospovidone	20.00
4.50	6	Magnesium Stearate	4.50

MANUFACTURING DIRECTIONS

1. The components, except for a portion of the magnesium stearate, are blended in a container mixer.
2. The blended material is sieved and preblended for an additional time period in a container mixer. The blended material is compacted using a roller compactor by applying a compaction force of 25–65 kN and a roller speed of 1.3–7.5 rpm.
3. The compacted material is sieved again and the remaining portion of the magnesium stearate is added and finally blended in a container mixer.
4. Then, 150 mg of the homogeneous mixture is filled in capsules, or compressed for tablets and subsequent coating.

Valsartan Capsules

Valsartan is a nonpeptide, orally active, and specific angiotensin II antagonist acting on the AT 1 receptor subtype. It is chemically described as *N*-(1-oxopentyl)-*N*-[[2'-(1 *H*-tetrazol-5-yl) [1,1'-biphenyl]-4-yl]methyl]-L-valine. It is available as capsules for oral administration, containing either 80 mg or 160 mg of valsartan. The inactive ingredients contained in the capsules are: cellulose compounds, crospovidone, gelatin, iron oxides, magnesium stearate, povidone, sodium lauryl sulfate, and titanium dioxide.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
80.00	1	Valsartan	80.00
1.50	2	Colloidal Anhydrous Silica Aerosil	1.50
31.50	3	Microcrystalline Cellulose Avicel	31.50
20.00	4	Polyvinylpyrrolidone Crospovidone	20.00
4.50	5	Magnesium Stearate	4.50

MANUFACTURING DIRECTIONS

1. The components, except for a portion of the magnesium stearate, are blended in a container mixer.
2. The blended material is sieved and preblended for an additional period of time in a container mixer. The blended material is compacted using a roller compactor by applying a compaction force of 25–65 kN and a roller speed of 1.3–7.5 rpm.
3. The compacted material is sieved again, and the remaining portion of the magnesium stearate is added and finally blended in a container mixer.
4. Then, 138.50 mg of the homogeneous mixture is filled in capsules or compressed for tablets and subsequent coating.

Vancomycin Hydrochloride Capsules

Vancomycin hydrochloride capsules contain chromatographically purified vancomycin hydrochloride, a tricyclic glycopeptide antibiotic derived from *Amycolatopsis orientalis* (formerly *Nocardia orientalis*). 500 mg of the base is equivalent to 0.34 mmol. Each capsule contains vancomycin hydrochloride equivalent to 125 mg (0.08 mmol) or 250 mg (0.17 mmol) vancomycin. The Pulvules also contain FD&C Blue No. 2, gelatin, iron oxide, polyethylene glycol, titanium dioxide, and other inactive ingredients.

Verapamil Hydrochloride Capsules

Verapamil is a calcium ion influx inhibitor (slow channel blocker or calcium ion antagonist). It is available for oral administration as a 360-mg hard gelatin capsule (lavender cap/yellow body), a 240-mg hard gelatin capsule (dark blue cap/yellow body), a 180-mg hard gelatin capsule (light gray cap/yellow body), and a 120-mg hard gelatin capsule (yellow cap/yellow body). These pellet-filled capsules provide a sustained release of the drug in the gastrointestinal tract. In addition to verapamil HCl, the capsule contains the following inactive ingredients: fumaric acid, talc, sugar spheres, povidone, shellac, gelatin, FD&C Red No. 40, yellow iron oxide, titanium dioxide, methylparaben, propylparaben, silicon dioxide, and sodium lauryl sulfate. In addition, the 240-mg and 360-mg capsules contain FD&C Blue No. 1 and D&C Red No. 28; and the 180-mg capsule contains black iron oxide.

MANUFACTURING DIRECTIONS

1. Verapamil hydrochloride (30 kg), malic acid (10 kg), and talc (2.4 kg) are blended and passed through a No. 100 mesh screen, using a conventional milling machine.
2. A polymer suspension is prepared containing 5% hydroxypropyl methylcellulose in methanol/methylene chloride 60/40.
3. Sugar/starch seeds (0.4–0.5 mm) (9 kg) are placed in a standard coating pan and rotation commenced.
4. The seeds are wetted with sufficient polymer suspension to dampen them thoroughly and then an amount of the powder blend is dusted on until no more adhered. This step is repeated until all the powder blend has been applied.
5. The coated seeds are allowed to dry after each application of polymer suspension.
6. When all of the powder has been applied, the coated seeds are dried at 40–60°C until all of the solvent has been driven off.
7. A membrane suspension is prepared from the following components: 2 parts by volume 5% hydroxypropyl methylcellulose in methanol/methylene chloride 60/40; 8 parts by volume 5% ethylcellulose in methanol/methylene chloride 60/40; and 5 parts by weight talc.
8. The coated seeds, which are prepared previously and which define the active core of the pellets being prepared, are placed in a coating pan and rotation commenced. The membrane suspension is applied to the coated seeds in separate coats, each coat corresponding to 10 ml of the membrane suspension per kg of coated seeds. After each coat had been applied, the pellets are air dried in the coating pan.
9. After the final coat has been applied, the pellets are dried at 40–60°C to evaporate all traces of solvent. Rapid release pellets as used in the controlled absorption pharmaceutical formulation of the invention are prepared by forming active cores without the subsequent application of a membrane thereto.

Verapamil Hydrochloride Sustained-Release Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
120.00	1	Verapamil Hydrochloride	120.00
20.00	2	Sucrose and Cornstarch Neutral Microgranules	20.00
11.30	3	Shellac, Bleached, Wax-Free	11.30
0.75	4	Eudragit L100	0.75
3.60	5	Eudragit L30D	3.60
1.23	6	Eudrafit NE30D	1.23
0.37	7	Diethyl phthalate	0.37
1.60	8	Talc	1.60
—	9	Alcohol	QS
—	10	Acetone	QS
—	11	Water Purified	QS

Note: For 240-mg strength, scale to twice the formula.

MANUFACTURING DIRECTIONS

1. The neutral microgranules (Item 2) are placed in a coating pan and pan started.
2. Prepare a 20% solution of Item 3 in a mixture of acetone and alcohol.
3. Set temperature of Step 1 to 25 ± 5°C. Apply shellac solution, alternating with Item 1 powder until all the active ingredient is incorporated.
4. Sieve microgranules through a 0.85-mm aperture. Dry microgranules at 30–40°C for 8 h.
5. Sieve dried microgranules and dry again at 30–40°C for 8 h.
6. Prepare a 15% alcoholic solution of Eudragit L100, and apply with talc; dry and apply until all solution is incorporated.
7. Sieve microgranules using a 1.18-mm aperture sieve.
8. Prepare an aqueous dispersion of Item 5 (L30D) and Item 7. Apply part of suspension to microgranules together with part of Item 8. Allow to dry. Repeat operation until desired dissolution rate is obtained.
9. Sieve microgranules using 1.18-mm sieve and then dry at 30–40°C for 12 h.
10. Prepare aqueous solution of NE30D and Item 7, apply in parts with remaining talc, and then dry. Repeat until desired dissolution rate is obtained.
11. Sieve using a 1.18-mm sieve. Dry at 30–40°C for 12 h.
12. Fill appropriate quantity based on assay. Use approximately 158.85 mg for 120-mg strength and 317.70 mg for 240-mg strength.

Vincamine Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
30.00	1	Vincamine	30.00
17.50	2	Lactose	17.50
166.80	3	Sucrose and Cornstarch Microgranules, Size 20	166.80
3.30	4	Polyvinyl Pyrrolidone	3.30
1.30	5	Shellac	1.30
3.60	6	Eudragit L	3.60
7.50	7	Talc	7.50
—	8	Alcohol	QS

MANUFACTURING DIRECTIONS

1. Charge Item 3 in a coating pan and run the pan.
2. Prepare solution of Item 4 in Item 8.
3. Add and mix Items 1 and 2 in a separate container.
4. Heat Step 1 to 25 ± 5°C; apply solution in Step 2, and alternate with powder mixture in Step 3 until all of Step 3 is incorporated.
5. Sieve granules through a 1.18-mm sieve in Step 4, and dry at 30–40°C for 8 h.
6. Prepare an alcoholic solution of Item 5 in Item 8, and apply to Step 5 until all incorporated.
7. Sieve microgranules through a 1.18-mm sieve and dry at 30–40°C for 8 h.
8. Prepare a solution of Item 6 in Item 8 and apply in steps until all solution is incorporated.
9. Sieve microgranules through a 1.18-mm sieve and dry at 30–40°C for 8 h.
10. Fill appropriate quantity in capsules; approximately 230 mg.

Vinpocetine Multiple Bead Capsules

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
160.00	1	Vinpocetine	160.00
		Powder Blend	
5.00	1	Vinpocetine	5.00
0.10	2	Sodium Lauryl Sulfate	0.10
3.0	3	Sodium Starch Glycolate	3.00
6.00	4	Glutamic Acid	6.00
7.00	5	Cornstarch	7.00
62.00	6	Lactose	62.00
13.00	7	Microcrystalline Cellulose	13.00
1.00	8	Magnesium Stearate	1.00
		pH Sensitive Coated Spheroid	
		Uncoated Spheroids (10% w/w Vinpocetine)	3.00 kg
		Methacrylic Acid Copolymer Type B Eudragit S	0.75 kg
		Triacetin	0.112 kg
		Isopropyl Alcohol	1.64 kg
		Methylene Chloride	1.99 kg
		Water	0.50 kg
		Coated Spheroids	
		Uncoated Spheroid (24% w/w Vinpocetine)	3.00 kg
		Hydroxypropyl Methylcellulose 2910, 4000 cps	0.075 kg
		Methylene Chloride	4.98 kg
		Methanol Anhydrous	2.96 kg
		Eudragit E30D Aqueous Dispersion	1.00 kg
		Calcium Stearate	0.03 kg
		Simethicone Emulsion	0.0025 kg
		Water Purified	0.50 kg

MANUFACTURING DIRECTIONS

1. Vinpocetine hydrochloride (10.0 kg), microcrystalline cellulose (Avicel-PH-101) (80.0 kg), and citric acid monohydrate (10.0 kg) are blended together in a 450-l planetary mixer. Water (100 kg) is added, and the mixer is run for 10 min until a homogeneous plastic mass is obtained. The mass is extruded under pressure through a perforated cylinder to give cylindrical extrudates of nominally 1 mm in diameter.
2. The damp extrudates (in batches of 15–20 kg) are placed in a spheronizer in which the rotating disc (diameter 68 cm) rotated at 300–400 rpm. The rotation is continued for 20 min, and the resulting spheroids are then dried at 80°C in a fluidized-bed drier. The dried spheroids are passed over a 1.2-mm. screen, and those that passed through are subjected to a 0.5-mm screen. The over- and undersized spheroids are discarded.
3. The finished dosage form consists of a hard gelatin capsule containing a powder blend of vinpocetine and two types of spheroids. The formulation particulars are based on 30 mg per capsule, although they can be designed to provide other dosage strengths.
4. The vinpocetine powder blend (or first group of spheroids) provides the loading dose, (e.g., 5 mg of vinpocetine).
   a. Blend the vinpocetine, lactose microcrystalline cellulose, starch, glutamic acid, sodium starch glycolate, talc triturate, and the sodium lauryl sulfate into the PK® blender for 20 min with intensifier bar running.
   b. Pass the Step 1 blend through a Fitz mill using a No. 1B screen, medium speed, knives forward.
   c. Return the granulation from Step 2 to the PK blender and add the magnesium stearate and blend for 2 min without the intensifier bar on.

5. The second and third types of spheroids are categorized as:
   a. pH sensitive coated spheroids to provide a second dose (pH > 6.5) (e.g., 12 mg vinpocetine). Uncoated spheroids are placed in a fluidized-bed coater. The Eudragit S solution is applied using a peristaltic pump. The spheroids are dried.
   b. Coated spheroids to provide a third dose (4–10 h post-ingestion) (e.g., 13 mg vinpocetine). Process for applying undercoat: The uncoated spheroids are placed in a fluidized-bed coater). Methocel E4MP solution is sprayed using a peristaltic pump. The spheroids are dried. Process for applying overcoat: Eudragit E30D suspension containing calcium stearate is sprayed on the methocel E4MP-coated spheroids using a peristaltic pump. The spheroids are dried.
6. Capsules are filled with the powder blend, pH sensitive coated spheroids, and coated spheroids on an encapsulating machine capable of dual filling powders and spheroids.

Vitamin B-Complex, Amino Acids, and Magnesium Effervescent Granules (Sugar-Free)

Bill of Materials

Scale (mg/Tab)	Item	Material Name	Qty/1000 Tabs (g)
2.00	1	Thiamin Hydrochloride	2.00
2.00	2	Pyridoxine Hydrochloride	2.00
5.00	3	Cyanocobalamin Dry Powder 0.1%	5.00
20.00	4	L-Glutamine	20.00
10.00	5	Inositol	10.00
10.00	6	Potassium L-Aspartate	10.00
500.00	7	DL-Carnitine Hydrochloride	500.00
350.00	8	Magnesium L-Aspartate	350.00
600.00	9	Citric acid, Anhydrous	600.00
500.00	10	Sodium Bicarbonate	500.00
QS	11	Flavors	QS
50.00	12	Kollidon VA 64	50.00
—	13	Isopropanol	80.00

MANUFACTURING DIRECTIONS

1. Mix Items 1–6, add the mixture of Items 7–12, granulate mixture of these two combinations with Item 13, pass through a 0.8-mm sieve, dry well, and mix.
2. Fill 2.1 g of the granules in sachets.

Vitamin B-Complex and Vitamin C Instant Granules

Bill of Materials			
Scale (mg/g)	**Item**	**Material Name**	**Qty/kg (g)**
3.60	1	Thiamine Hydrochloride	3.60
5.70	2	Riboflavin Phosphate Sodium	5.70
45.00	3	Nicotinamide	45.00
4.50	4	Pyridoxine Hydrochloride	4.50
15.00	5	Cyanocobalamin, Gelatin Coated 0.1%	15.00
150.00	6	Ascorbic Acid, Powder	150.00
723.00	7	Sucrose	723.00
51.00	8	Kollidon 30	51.00
QS	9	Ethanol	180 ml

MANUFACTURING DIRECTIONS

1. Mix Items 1–7, granulate with solution of Items 8 and 9, dry, and pass through a 0.8-mm sieve.
2. Fill 1 g of the granules in sachets, which corresponds to two daily vitamin B and vitamin C requirements of adults.

Vitamin C and Calcium Carbonate Effervescent Tablets

Bill of Materials			
Scale (mg/Tab)	**Item**	**Material Name**	**Qty/1000 Tabs (g)**
300.00	1	Calcium, USE Calcium Carbonate	315.00
450.00	2	Sodium Tartaric Acid, Powder Bicarbonate	450.00
600.00	3	Kollidon 30	600.00
35.00	4	Kollidon 30	35.00
200.00	5	Isopropanol	200.00
400.00	6	Sucrose Crystalline	400.00
500.00	7	Ascorbic Acid, Crystalline, with Excess	550.00
120.00	8	Kollidon CL	120.00
60.00	9	Polyethylene Glycol 6000, Powder	60.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of Items 1–3 with solution of Items 4 and 5, mix with Item 6, and dry.
2. Add Items 7–9 and press with a high compression force at maximum 30% of relative atmospheric humidity.
3. Compress 2500 mg in 20 mm biplanar punches.

Zanamivir Powder

The chemical name of zanamivir is 5-(acetylamino)-4-[(aminoimino-methyl)-amino]-2,6-anhydro-3,4,5-trideoxy-D-glycero-D-galacto-non-2-enonic acid. It is for administration to the respiratory tract by oral inhalation only. Each disc contains 4 regularly spaced double-foil blisters with each blister containing a powder mixture of 5 mg of zanamivir and 20 mg of lactose. The contents of each blister are inhaled using a specially designed breath-activated plastic device for inhaling powder called the DISKHALER®.

Bill of Materials			
Scale (mg/Disk)	**Item**	**Material Name**	**Qty/1000 Disks (g)**
5.00	1	Zanamivir	5.00
20.00	2	Lactose Anhydrous	20.00

The drug is also administered as aqueous solution (10%) with 0.04% benzalkonium chloride and 0.40% phenylethyl alcohol. In an aqueous cosolvent system, it contains 10% active drug, 0.04% benzalkonium chloride, 10% PEG 400, and 30% propylene glycol (balance purified water). In an aerosol formulation, there is 7.5% active drug, 25.6% propellant 11, and 66.5% propellant 12.

Zidovudine Capsules

Zidovudine (formerly called azidothymidine [AZT]), a pyrimidine nucleoside analog active against HIV. Each capsule contains 100 mg of zidovudine and the inactive ingredients cornstarch, magnesium stearate, microcrystalline cellulose, and sodium starch glycolate. The 100-mg empty hard gelatin capsule, printed with edible black ink, consists of black iron oxide, dimethylpolysiloxane, gelatin, pharmaceutical shellac, soya lecithin, and titanium dioxide. The blue band around the capsule consists of gelatin and FD&C Blue No. 2.

Bill of Materials			
Scale (mg/Cap)	**Item**	**Material Name**	**Qty/1000 Caps (g)**
100.00	1	Zidovudine (3′-Azido-3′-Deoxythymidine)	100.00
200.00	2	Lactose	200.00
50.00	3	Cornstarch	50.00
5.00	4	Polyvinylpyrrolidone	5.00
4.00	5	Magnesium Stearate	4.00

MANUFACTURING DIRECTIONS

1. Sieve Items 1–4 through 80-mesh sieve and blend.
2. Pass Item 5 through a 100-mesh sieve, and add to Step 1 and blend for 2 min.
3. Fill 359 mg in capsules.

Zinc Oxide and Cornstarch Powder

Cornstarch baby powder combines zinc oxide (10%) with topical starch (cornstarch) for topical application. Also contains: fragrance and tribasic calcium phosphate.

Ziprasidone Hydrochloride Capsules

Ziprasidone hydrochloride is an antipsychotic agent that is chemically unrelated to phenothiazine or butyrophenone antipsychotic agents. It has a molecular weight of 412.94 (free base), with the following chemical name: 5-[2-[4-(1, 2-benzisothiazol-3-yl)-1-piperazinyl]ethyl]-6-chloro-1,3-dihydro-2 *H*-indol-2-one. Capsules contain a monohydrochloride, monohydrate salt of ziprasidone. Chemically, ziprasidone hydrochloride monohydrate is 5-[2-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]ethyl]-6-chloro-1,3-dihydro-2 *H*-indol-2-one, monohydrochloride, monohydrate. Capsules are supplied for oral administration in 20 mg, 40 mg, 60 mg, and 80 mg doses. Capsules contain ziprasidone hydrochloride monohydrate, lactose, pregelatinized starch, and magnesium stearate.

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
20.00	1	Ziprasidone, USE Ziprasidone Hydrochloride	22.65
66.10	2	Lactose Monohydrate	66.10
10.00	3	Pregelatinized Cornstarch	10.00
0.75	4	Magnesium Stearate	0.75

MANUFACTURING DIRECTIONS

1. Pass Items 1–3 through 80-mesh screen and blend.
2. Pass Item 4 through 100-mesh screen, and add and blend for 2 min.
3. Fill in size 4 capsules (100 mg). For higher strengths, scale up the quantity and size of capsule. The lactose monohydrate weight is adjusted according to small potency changes in the ziprasidone hydrochloride monohydrate in order to maintain a constant capsule weight.

Zonisamide Capsules

Zonisamide is an antiseizure drug chemically classified as a sulfonamide and unrelated to other antiseizure agents. The active ingredient is zonisamide, 1,2-benzisoxazole-3-methanesulfonamide. It is supplied for oral administration as capsules containing 100 mg zonisamide. Each capsule contains the labeled amount of zonisamide plus the following inactive ingredients: microcrystalline cellulose, hydrogenated vegetable oil, sodium lauryl sulfate, gelatin, and colorants.

Bill of Materials

Scale (mg/Cap)	Item	Material Name	Qty/1000 Caps (g)
100.00	1	Zonisamide	100.00
35.00	2	Lactose Anhydrous	35.00
17.00	3	Cornstarch	17.00
40.00	4	Crystalline Cellulose	40.00
6.00	5	Hydroxypropyl Cellulose	6.00
1.00	6	Light Anhydrous Silicic Acid	1.00
1.00	7	Magnesium Stearate	1.00
QS	8	Water Purified	QS

MANUFACTURING DIRECTIONS

1. Among the preceding components, zoniamide, lactose, cornstarch, and crystalline cellulose are blended, and thereto is added hydroxypropyl cellulose being dissolved in water. The mixture is kneaded, dried, and granulated.
2. To these granules are added magnesium stearate and light anhydrous silicic acid, and the mixture is filled (200 mg) in each capsule.
3. A 20% powder formulation contains:

   Zonisamide, 200 g
   Lactose, 719 g
   Hydroxypropyl cellulose, 20 g
   Light anydrous silicic acid, 1 g
   Total, 940 g
4. Using a high-shear granulator, all the preceding components for powder formulation are blended, sprayed with an ethanolic solution (200 g) containing ethylcellulose (40 g) and hydroxypropyl cellulose (20 g) for granulation, and are then made into granules. These are dried and regulated in size to give 20% powders.